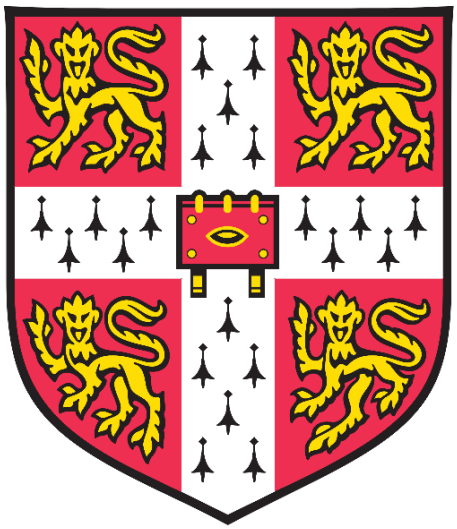
Phenotypic variation and thermoregulation of the human hand



This dissertation is submitted for the degree of Doctor of Philosophy

November 2018

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The hand has the highest surface area-to-volume ratio of any body part. This property offers the potential for the hand to serve an important function in thermoregulation through radiative heat loss. Theoretically, the capacity for heat loss may be influenced by hand and digit proportions, but the extent to which these proportions influence the hand's radiative properties remains under-investigated. Although hand morphology is highly constrained by both integration and functional dexterity, phenotypic variation in hand and digit proportions across human populations shows broad ecogeographic patterns. These patterns have been associated with climate adaptation. However, the theory linking climate adaptation to such ecogeographic patterns is based on underlying assumptions relating to thermodynamic principles, which have not been tested *in vivo*. This study sought to determine the influence of hand and digit proportions on heat loss from the hands directly, the additional anthropometric factors that may affect this relationship, and the impact of variation in hand proportions on dexterity in the cold.

The relationship between hand proportions and thermoregulation was tested through both laboratory-based investigation and a field study. The laboratory investigation assessed the relationship between hand proportions and heat loss, the influence of body size and composition on this relationship, and the effect of morphological variation on manual dexterity. Participants (N=114; 18-50 years of age), underwent a 3-minute ice-water hand-immersion.

Thermal imaging analysis was used to quantify heat loss. Hand and digit proportions were quantified using 2D and 3D scanning techniques; body size and composition were measured using established anthropometric methods and bio-impedance analysis. After accounting for body size, hand width, digit-to-palm length ratio, and skeletal muscle mass were significant predictors of heat loss from the hand, whilsthand length and fat mass were not. A separate set of participants (N=40) performed a Purdue pegboard dexterity test before and after the immersion test, which demonstrated that digit width alone negatively correlated with dexterity.

The field study tested whether phenotypic variation in upper limb proportions could be attributed to cold adaptation or selection for dexterity in living populations exposed to significant energetic stress. Upper limb segment lengths were obtained from participants (N=254; 18-59 years of age), from highland and lowland regions of the Nepalese Himalayas using established anthropometric methods, and relative hand proportions were assessed in relation to severe energetic stress associated with life at high altitude. Relative to height, hand length and hand width were not reduced with altitude stress, whilst ulna length was. This indicates that cold adaptation is not shaping hand proportions in this case, although phenotypic variation in other limb segments may be attributed to cold adaptation or a thrifty phenotype mechanism.

The current study provides empirical evidence to support the link between surface area-to-volume ratio, thermodynamic principles and ecogeographical patterns in human hand morphology. However, this research also demonstrates the complexity of the hand's role in thermoregulation; not only do other factors such as muscularity affect heat loss from the hand, but hand morphology is also highly constrained by integration and dexterity.

Declaration

This dissertation is the result of my own work and includes nothing that is the outcome of work done in collaboration except as declared here. All results chapters (Chapters 3-6) of this dissertation have been accepted for publication. Contributions to the publications comprising Chapters 3-5 were made by co-authors Dr Jay Stock, my doctoral supervisor, and Dr Alison Macintosh, my doctoral adviser. Their co-authorship reflects their input into the design of my PhD project and their advisory role during the writing of each research article. The co-authors of the publication comprising Chapter 6 were Dr Jay Stock, Dr Alison Macintosh, Dr Rajendra Kumar BC, and Dr Emma Pomeroy. As with the earlier chapters, Dr Jay Stock and Dr Alison Macintosh advised me on this final results chapter during the writing process; Dr Rajendra Kumar BC assisted in the logistical aspects of the field study reported in this chapter, and Dr Emma Pomeroy advised me on the design and implementation of the field methods reported in this chapter.

This dissertation is not substantially the same as any that I have submitted, or is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution. I further state that no substantial part of my dissertation has already been submitted, or is being concurrently submitted, for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution.

This dissertation does not exceed the prescribed word limit for the Archaeology and Anthropology Degree Committee (80,000 words).

Stephanie Payne
Cambridge, 2018

Acknowledgements

I would like to thank Jay Stock for his invaluable guidance through my PhD journey. From the outset, Jay's ability to provide direction in the tumult of academic ideas put me at ease and kept me on the straight and narrow. Whenever I felt a loss of direction during the project, Jay has always been able to find a worthy point of refocus, and often broadened my perspective on research possibilities. Jay's constant ability to inspire and renew my excitement about anthropology has been such a great source of encouragement. Thanks to Jay, the PAVE research group have redefined "Taking care of business".

I am forever indebted to Ali Macintosh for the incredible support she has given me with this research. When I first met Ali, I was awe-inspired by a woman whose hardworking attitude had led her through great research success, and I wanted to follow in her footsteps. Ali has always been present to advise me through every stage of my research, on every aspect from ethics forms to evolutionary hypotheses. Not only has she provided vital feedback on the writing of draft publications, she has also been an invaluable companion in the lab, keeping me company on a daily basis while we waited for our respective participants. Her good humour and can-do attitude continue to inspire me, and I am incredibly grateful for all the time and energy that she has given to help me.

The PAVE research group are a truly incredible bunch and have been fantastic colleagues and friends. It fills me with great comfort to know that strong, passionate women such as Sarah-Louise are at the forefront of women in science; she has encouraged me to become more comfortable with who I am. Not only has her strength of character been a guiding light, but her committed attendance in the office has made it all the easier to come to work every day. Jaap's relaxed and happy nature has been such a calming positive influence in times of uncertainty. He has been a willing pilot-test subject, a particularly

mean feat considering he willingly plunged his hands into ice water on multiple occasions in the name of science. Michael's affinity for science communications has taught me so much about the best ways to disseminate my research: opening my eyes to the Twittersphere has been an exciting, if not nerve-racking experience. Having started the PhD journey with Eoin, his empathy for the challenges we have had to face along the way has made everything easier. Ella's determination and ever cheerful nature has infused so much energy into daily office life, and she is the most fantastic person to bounce ideas off. The support from the postdocs, Laura, Danny, and Emma, has been invaluable, both in advising me on standard scientific protocol and anthropometric measures, but also about remaining positive through the writing process. I feel truly lucky to call myself a member of such an awesome research group.

Away from the office, there have also been many important collaborators who made field work possible. Not only did Dr Andrew Murray make the decision to award me the Trinity Hall Studentship, but he also offered me the most incredible opportunity to collaborate with Xtreme Everest on the research trip to the Himalayas. His unfaltering support has been truly heart-warming. The collaborators during the fieldwork were relentless in their hard work. Tsering our translator, a Tibetan refugee, is one of the most inspiring women I have ever met. Despite being exiled since birth and forced to live in poverty, she risks her life travelling to India every year to attend university to train as a nurse to help her community. I wish to thank her for the incredible work she did for us. It was a joy to return every day to our generous hosts in the Himalayas, Lhakpa Sonam Sherpa and his wife Nima, after long bouts of data collection. They made us feel like royalty, plying us with homemade Sherpa chang and potato pancakes every day. Their kindness was overwhelming.

The financial support from Trinity Hall has enabled me to fully embrace PhD life without financial concerns. The additional funding support for fieldwork and conference attendance from the Department of Archaeology, the Sigma Xi Scientific Research Society, the British Association for Biological Anthropology and Osteoarchaeology, The Cambridge Philosophical Society, and National Geographic has opened up so many opportunities for my research. I should also like to make a special mention of the amazing team at National Geographic, particularly Claire Mcnulty, for inviting me to their incredible Explorers festival, teaching me so many valuable skills, and opening my eyes to new avenues of research.

This research would not have been possible without the generosity of all the volunteers who took part in both the laboratory and field studies. The knowledge that over 200 people willingly agreed to plunge their hands into freezing cold water for my research is truly humbling. It gave me faith in humanity's curiosity. Furthermore, their ability to not utterly detest me after subjecting them to freezing pain after the experiment is somewhat remarkable. The enthusiasm of the field participants was also heart-warming. Their excitement at having themselves and their friends measured was highly entertaining - an inadvertent competition - that became quite a spectacle.

Away from the field, all of my family members have been absolute strongholds of support. Both of my brothers, Duncan and Patrick, have been keen listeners, and inspiring in their relentless determination to succeed in their own work. I am truly humbled to be their sister. Mum and Dad, with their own challenges to face, have been ever supporting of my PhD work; no matter how menial the question or small the problem, they are always there to listen and help.

The Cambridge University Women's Lightweight Boat Club have provided great respite from the endless research grind. Never has it been so easy to wake up at 5am day

after day, to get on an icy cold river, in wind and rain, and be berated by coaches. It was a pleasure being part of a team of women who pushed each other beyond the limit every day and showed me that no matter how difficult the challenge, you can throw yourself at it and come out on top. They taught me to be humble, to embrace every challenge, to regret nothing, and that a team of women is unstoppable. I feel very fortunate to be part of the most successful Cambridge rowing squad in 25 years.

And finally, I want to thank Oli, to whom this PhD is dedicated. Your all-encompassing energy emanates through everything you do, and is such a positive influence on everyone around you. Coming home to your friendly face is always the highlight of my day. You make me feel energised with just a smile. You support me, challenge me, and have helped me to see so much more of the world. When I lost momentum in the Himalayas, you drove my research forward. It felt like you took every step for me. Your persistence for "just a few more data points" at every village ensured that I collected sufficient data. Obtaining those valuable field results would not have been possible without you. You always put me first and I am forever indebted to you for it. Thank you.

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Chapter 1

Introduction

"The hands are the instruments of man's intelligence"

Maria Montessori

With its dextrous abilities, the human hand is often perceived as integral to our evolutionary success and cultural complexity (Lemelin and Schmitt, 2016). This popular view of the hand as a uniquely specialised tool has led to a considerable amount of scientific literature devoted to the discussion of the evolution of the human hand and its dexterity (Napier, 1960; Napier and Napier, 1967; Marzke and Shackly, 1986; Marzke and Marzke, 1987, 2000; Boesch and Boesch, 1993; Marzke and Wullstein, 1996; Tocheri et al., 2003; Tocheri, 2007; Feix et al., 2015; Key and Dunmore, 2015; Kivell, 2015; Williams-Hatala et al., 2018; Hu et al., 2018). Undoubtedly, many aspects of our behaviour are dependent on manual dexterity facilitated by our hand morphology, but only relatively recently have we acknowledged the developmental constraints that act on hand morphology and its integration into the body system (Rolian, 2009, 2016; Rolian et al., 2010; Williams-Hatala, 2016). Furthermore, there is still a key aspect of hand biology that remains understudied by anthropologists: the role of the human hand in thermoregulation (Taylor, 2014). As the region of the body with the highest surface area-to-volume ratio, the hand has the greatest capacity to facilitate heat radiation per unit area (Molnar, 1957; Hirata et al., 1993). This property may have been relevant for hominin evolution in tropical regions, particularly with increasing demand for thermoregulatory adaptations with the evolution of long-distance running (Bramble and Lieberman, 2004; Steudel-Numbers et al., 2007; Steudel-Numbers and Wall-Scheffler, 2009). However, as human populations

expanded into a more diverse range of climates, the radiative properties of the hand may have provided more of a challenge to maintaining temperature of the hand and digits (Wells and Stock, 2007). The development of clothing may have alleviated these thermoregulatory challenges to some extent (Gilligan, 2010), but the hands would have remained exposed during manual tasks essential for survival (Heus et al., 1995), and thus the hands would still be susceptible to heat loss and destabilising thermoregulation.

The current study seeks to explore the concept of the hand as a thermoregulatory tool, and how this may relate to other aspects of hand biology, including dexterity and morphological integration. This thesis will begin by reviewing evidence for thermoregulatory adaptations in the human hand.

1.1. Thermoregulatory adaptations of the human hand

To fully utilise the high surface area-to-volume ratio for heat loss, enhancement of several thermoregulatory mechanisms has occurred in the hand to optimise evaporation, convection, conduction, and radiation (Taylor, 2014) (Figure 1.1). The hands are optimised for evaporative heat loss as they have the highest eccrine sweat gland density of any body part: approximately 500-600 eccrine glands per cm^2 on the palms, compared to approximately 100 per cm^2 on the torso and 200 per cm^2 on the forehead (Taylor and Machado-Moreira, 2013). The sensitivity and sweat production rate of these palmar sweat glands increases with prolonged exposure to high environmental temperature, while torso sweat glands decrease in relative sweat rate (Allan and Wilson, 1971; Ethan et al., 1971; Chen and Elizondo, 1974; Buono, 2000). This thermoregulatory shift in sweat rate from the torso to the peripheries is an essential acclimatisation trait in hot climates, enabling the hands to be largely responsible for thermoregulatory heat loss (Périard et al., 2015). Sweat evaporation is more effective with constant air flow (Adams et al., 1992); the swing of the arms during bipedal locomotion promotes air flow around the upper limbs, thus further

promoting heat loss from the hands, which have the greatest displacement value, and therefore the greatest air flow rate surrounding them (Cross et al., 2008). The combination of high surface area-to-volume ratio, arm swing, and high sweat gland density optimises the hands for radiative, evaporative, and convective heat loss, demonstrating the crucial role the hands play in thermoregulation.

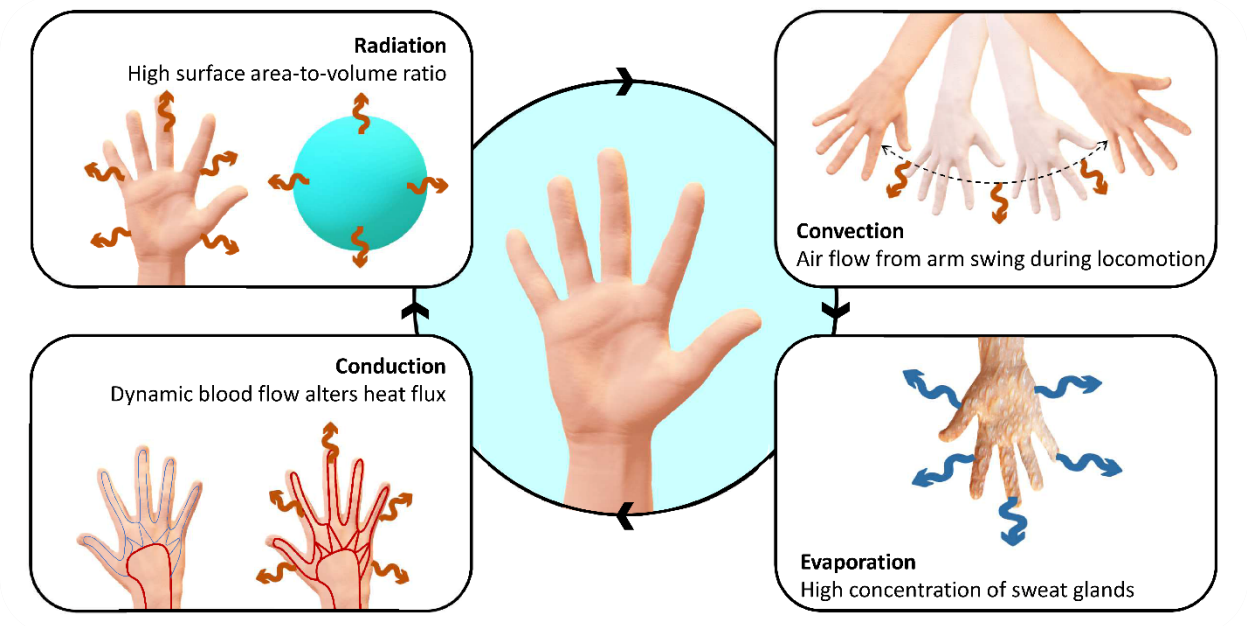


Figure 1.1 Summary of thermoregulatory adaptations of the hand

In addition to radiation, evaporation, and convection, the hands are also able to change their heat-conducting capacities through vasoregulation, or dynamic blood flow. Changes in blood flow to the surface of the hand will alter the extent of heat conduction to the peripheries (Johnson and Proppe, 1996), and thus can be an effective form of thermoregulation. If a change in core body temperature or skin temperature is detected by the sensory nervous system, sympathetic vasoregulator nerves are activated to alter the contraction of smooth muscle around the vessels leading to a dense network of papillary capillaries at the surface of the skin in the extremities (Zhong et al., 2000; Standring, 2008; Charkoudian, 2010). Relaxation of smooth muscle around the vessels leading to these

capillaries can increase blood flow through the digits up to 8 L/min (Rowell, 1974; Johnson and Proppe, 1996), allowing transmission of heat via the blood to the peripheries, which is then conducted to the surface of the skin and removed via radiation or evaporation. Conversely, constriction of the smooth muscle results in a flow rate close to zero in the digits, significantly reducing heat flux from the body's outer shell (Sessler et al., 1990; Charkoudian, 2010). In cold conditions, this vasoregulation is even more nuanced to prevent potential injury from long-term reduced blood flow in the extremities; a post-vasoconstriction response can occur known as cold-induced vasodilatation (CIVD) (Lewis, 1930; Daanen, 2003), which allows a rapid temporary influx of blood into the peripheral tissues to increase digit temperature and prevent long-term cold injury, such as frostbite (Fox and Wyatt, 1962; Bergersen et al., 1999). Overall, this complex vasoregulation is another key adaptation which exploits the high surface area-to-volume ratio of the hand, further augmenting the essential role of the hands in thermoregulation.

Thus, the hand is, theoretically, of great adaptive value for thermoregulation, particularly in hot climates, due to its radiative, evaporative and convective capacities. However, human populations span a vast range of climates (Wells and Stock, 2007), and thus differential adaptations are required to maintain thermal balance across different populations. Other than physiological acclimatisation of sweating and vasoregulation mechanisms, human populations may have evolved optimal hand proportions for their environment.

1.2. Ecogeographical patterns in human hand morphology

Research based upon the quantification of hand proportions in skeletal remains has indicated that there are ecogeographic patterns in hand morphology, whereby the first metacarpal (Betti et al., 2015), and second metacarpal (Lazenby and Smashnuk, 1999), are shorter relative to body size in populations inhabiting cold regions compared to those

inhabiting temperate and tropical regions. Lazenby and Smashnuk (1999) observed that the second metacarpal of an Inuit population from Southampton Island was significantly shorter in length and broader at the base relative to a sample from European settlers. Similarly, Betti *et al.* (2015) found that the ratio between the maximum breadth of the distal epiphysis and maximum length of the first metacarpal increased with decreasing minimum temperature across skeletal populations from across the globe. These findings correspond to patterns observed in both radial and tibial proportions, where reduction in length of the distal limb segment is associated with lower environmental temperatures (Ruff, 1994; Holliday, 1999; Holliday and Ruff, 2001; Temple and Matsumura, 2011). These ecogeographical patterns found in limb morphology, in conjunction with patterns of increasing body mass (Roberts, 1953; Ruff, 1994; Katzmarzyk and Leonard, 1998), and body breadth with decreasing environmental temperature (Ruff, 1993, 1994; Holliday, 1997a; Holliday and Hilton, 2010), have been used as evidence to support the theory of cold adaptation, based on the ecogeographical rules laid out by Bergmann[1] and Allen (Bergmann, 1847; Allen, 1877). These ecogeographical rules associate climate with body size (Bergmann, 1847) and limb proportions (Allen, 1877), based on the physical laws of thermodynamics; a body with a large surface area-to-volume ratio will result in increased heat loss to its surroundings (Scholander et al., 1950). As the hand is the body element with the largest surface area-to-volume ratio, it has the greatest potential for heat loss, and thus may have a strong thermoregulatory selective pressure acting upon it. Variation in the first and second metacarpal, do appear to align with Allen's rule (Lazenby and Smashnuk, 1999; Betti et al., 2015). However, the conclusion that digit proportions are shaped by climate should be treated with caution as the presence of these ecogeographical patterns in *Homo*

[1] A translation by Carl Godfrey (2004) of Bergmann's (1847) *Über die Verhältnisse der Wärmeökonomie der Thiere zu ihrer Größe* was used during the writing of this thesis. The original text is cited throughout.

sapiens has been widely questioned. Although evidence for these ecogeographical patterns is seen in many species across mammals (Paterson, 1996; Ashton et al., 2000; Blackburn and Hawkins, 2004; Blackburn et al., 2008), birds (Ashton, 2002; Meiri and Dayan, 2003), and some reptiles (Ashton and Feldman, 2003), patterns previously observed in humans are less pronounced than previously thought (Foster and Collard, 2013).

1.2.1. Limitations surrounding climate adaptation assumptions

Since Roberts' (1953) seminal work presenting evidence for Bergmann's rule in humans, further investigation has brought the concept of human climate adaptation under scrutiny. Foster and Collard (2013) demonstrated that Bergmann's rule was only applicable when populations span at least of 50° latitude or a 30°C temperature difference. Furthermore, they discovered a sampling bias towards the northern hemisphere so that when data from each hemisphere were analysed separately, Bergmann's rule did not apply to southern hemisphere populations. Further statistical analysis has weakened support for Bergmann's rule; when assessing limb proportions and body breadth, multivariate cluster analysis groups Inuit and European populations together relative to sub-Saharan African groups, despite Inuit experiencing significantly lower temperatures than Europeans (Holliday and Hilton, 2010). The ambiguity of ecogeographic patterns in humans is likely to stem from multiple causes: migratory events often complicate patterns in limb proportions based on geographic position (Holliday, 1997a, 1999); secular trends in nutrition (Katzmarzyk and Leonard, 1998), particularly nutrition availability during early life, appear to be stronger predictors of body size and shape than climate variables (Hadley and Hruschka, 2014; Stulp and Barrett, 2014); finally increased use of clothing over time has reduced climate-associated trends in body variables, such as the narrowing of the femoral neck shaft angle with decreasing minimum temperature (Gilligan et al., 2013). Analysis of population structure indicates that genetic drift can explain a considerable amount of

variation in human body shape and limb proportions, potentially more so than climatic selective pressures (Roseman and Auerbach, 2015; Savell et al., 2016). Genetic drift over increasing geographic distance can produce a gradient in a given trait, which is entirely unrelated to selective forces; the pattern produced is known as spatial autocorrelation, and is observed in genetic data (Relethford, 2009), cranial anatomy (Harvati and Weaver, 2006; Manica et al., 2007; von Cramon-Taubadel and Lycett, 2008; Betti et al., 2009), pelvic anatomy (Betti et al., 2013), and long bone morphometrics (Savell et al., 2016).

Although spatial autocorrelation is not observed when investigating phenotypic variation in first metacarpal proportions (Betti et al., 2015), it brings to light the potential role of genetics in shaping patterns in hand proportions. The hands are morphologically integrated into the whole body system (Rolian, 2009), and may be pleiotropically constrained by coevolution with the human foot through their joint developmental origin and control via Homeobox genes (Rolian et al., 2010). Analysis of phenotypic covariation indicates that strong selection acting to shorten the lateral phalanges of the foot for bipedalism facilitated changes in hand phalanges through genetic pleiotropic effects, resulting from a single gene controlling extremity traits in multiple appendages (Rolian et al., 2010). The similarity in developmental architecture between the hands and feet provides support for this theory. Hand morphology may well be an "evolutionary spandrel" (Gould and Lewontin, 1979), whereby changes in the foot have also led to changes in the hand as a result of pleiotropy, and hand morphology has since been exapted for tool use and other manual tasks (Gould and Vrba, 1982). Whether the hands are exapted or not, there appear to be significant developmental constraints which limit variation in human hand proportions.

Indeed, hand proportions are highly conserved even when exposed to significant energetic stress during development (Pomeroy et al., 2012). This has been explained as a

plastic response to limited energy during growth, whereby energetic investment is prioritised in body elements adapted for specific important behaviours, such as the hands for dexterity, at the expense of other limb segments. Whilst this particular pattern has only been found in one energetically stressed population (Pomeroy et al., 2012), and requires further testing, it is indicative of the preservation of hand dimensions even under developmental energetic stress. This suggests that the morphology of the hand is highly conserved and that minimal intraspecific variation occurs through energetic limitations during development.

Intraspecific phenotypic variation in human hand morphology that does occur is either created by nuances in gene expression (Wray, 2007; Carroll, 2008), or responses to developmental environment independent of energy availability. For example, differences in steroid hormone exposure during growth and development are also known to influence digit dimensions (Ecker, 1875; George, 1930; Manning et al., 1998; McFadden and Shubel, 2002; Lutchmaya et al., 2004). Hand proportions may also change through plastic responses to the habitual use of the hand throughout life. For example, hand width is seen to differ with handedness (Krishan and Sharma, 2007), and long-term manual use can significantly increase the size of muscle tissue within the palm, again resulting in increases in hand width within an individual's lifetime (Saengchaiya and Bunterngchit, 2004; Furuya et al., 2011). Changes in hand morphology as a response to tool use and biomechanical loading may also have the potential to occur over a longer, multi-generational time frame (Williams-Hatala et al., 2018). Thus, there are many factors to account for when attempting to determine the origin of phenotypic variation in the human hand. Whether climate adaptation does play a role here remains to be seen.

1.3. Testing assumptions surrounding climate adaptation

The application of climate adaptation theory to the human hand makes a key assumption – that the hand is a passively radiating object where heat loss is directly proportional to surface area-to-volume ratio (Scholander et al., 1950). However, it is unlikely that heat loss from the hand will follow a straightforward surface area-to-volume ratio rule; the physiological thermoregulatory mechanisms (Figure 1.1) will significantly alter the hand's heat loss capacities in hot and cold conditions, which may negate any influence that surface area-to-volume ratio alone would have (Steegmann, 2007). Thus an essential assumption surrounding the applicability of climate adaptation theory to the hands remains to be tested: do hand proportions directly influence heat loss from the hand?

1.3.1. A whole-body system approach

Tackling this question requires a biological systems approach, as the hand is not an isolated entity, but an element integrated into a complex body system. When testing heat loss from the hand, factors affecting whole-body thermoregulation, such as thermogenesis and insulation, should also be taken into account to assess their influence on hand temperature. Thermal balance is influenced by the insulative and thermogenic properties of different tissues (Fournet et al., 2013; Marins et al., 2014), and thus heat flux throughout the body, including the extremities, may be affected by body composition.

When examining heat loss from the extremities, body size may also be an important influence, based on the thermodynamic assumptions used to explain cold adaptation theory, as discussed previously (Ruff, 1994). In turn, body size may affect heat flux in the extremities (Havenith, 2001; Daanen, 2003; Chudecka, 2013), due to the dynamic nature of the whole-body system. Understanding the role of whole-body properties in heat loss from

the extremities will, in turn, inform analysis of the relationships between hand temperature and other manual properties.

1.3.2. Implications for dexterity

Establishing the influences of body size, body composition, and hand dimensions on heat loss from the hand during cold exposure will have implications for understanding dexterity in cold conditions. Dexterity is known to be significantly compromised during cold exposure (Horvath and Freedman, 1947; Teichner, 1957; Gaydos and Dusek, 1958; Clark, 1961). However, the influence of hand proportions on retention of dextrous abilities in cold conditions is currently unknown. Understanding this relationship will provide insight into the validity of cold adaptation theory applied to the hands, as the hands will likely be exposed when carrying out dextrous tasks, and therefore selection may act to promote the retention of dexterity for essential survival tasks.

1.3.3. Implications for interpreting hominin morphology

Understanding the relationship between hand proportions and dexterity in cold conditions may provide insight into the dextrous abilities of extinct hominins in challenging climatic conditions. As we become increasingly aware of the dextrous capacities of extinct hominins (Niewoehner et al., 2003; Niewoehner, 2006; Feix et al., 2015; Skinner et al., 2015; Hoffmann et al., 2018), it is important to be able to put this into a climatic context. Assessing whether morphology may have related to dexterity in specific climatic conditions in extinct hominins is only possible by considering modern day analogues. However, these inferences should also be treated with caution as it is not possible to infer the physiological adaptations extinct populations may have had, and physiology plays a significant role in dexterity changes in cold conditions.

1.4. Summary

In summary, phenotypic variation in the human hand is relatively constrained, both by potential morphological integration with the feet and upper limb, and also by function in the form of dexterity. Some of the limited variation in elements of the human hand has been attributed to cold adaptation, but this has yet to be tested *in vivo*. Understanding the relationship between hand and digit dimensions and heat loss from the hand as part of a dynamic body system will test whether the principles underlying cold adaptation theory are applicable to the hand. This may also have implications for interpreting the maintenance of dexterity in cold conditions, and whether this played a possible role in shaping the hands of extinct and extant hominins.

1.5. Purpose and Outline of the current study

1.5.1. Purpose

The purpose of the current study is to assess whether hand and digit proportions influence heat loss from the hands *in vivo*, to determine whether the underlying assumptions of Allen's rule are applicable to the hands. This will be observed in the broader context of the whole-body system, and how body size and body composition may affect heat loss from the hands. In turn, the implications for dexterity and heat loss are considered. Whether ecogeographical patterns can be found in a population exposed to multiple stresses will also be tested, to assess the applicability of cold adaptation theory in a multi-stress context.

1.5.2. Outline

This thesis, as a collective whole, investigates phenotypic variation of the human hand in light of cold adaptation theory. It is structured in a series of distinct publications, each with its own introduction, results, and discussion. In each chapter, the introduction

expands upon the brief introduction found here (Chapter 1), which has outlined the key rationale for this research. The current chapter is followed by two discrete sections. Part I (Chapters 2-5) reports on a series of laboratory experiments investigating *in vivo* heat loss from the hand and its associations with hand proportions, body size and composition, and dexterity (Figure 1.2); Part II (Chapter 6) reports on a field study assessing phenotypic variation in Himalayan populations and how this may be attributed to cold adaptation or other forms of energetic stress. Parts I and II are followed by a general discussion (Chapter 7), which summarises the findings and considers the broader implications of this research.

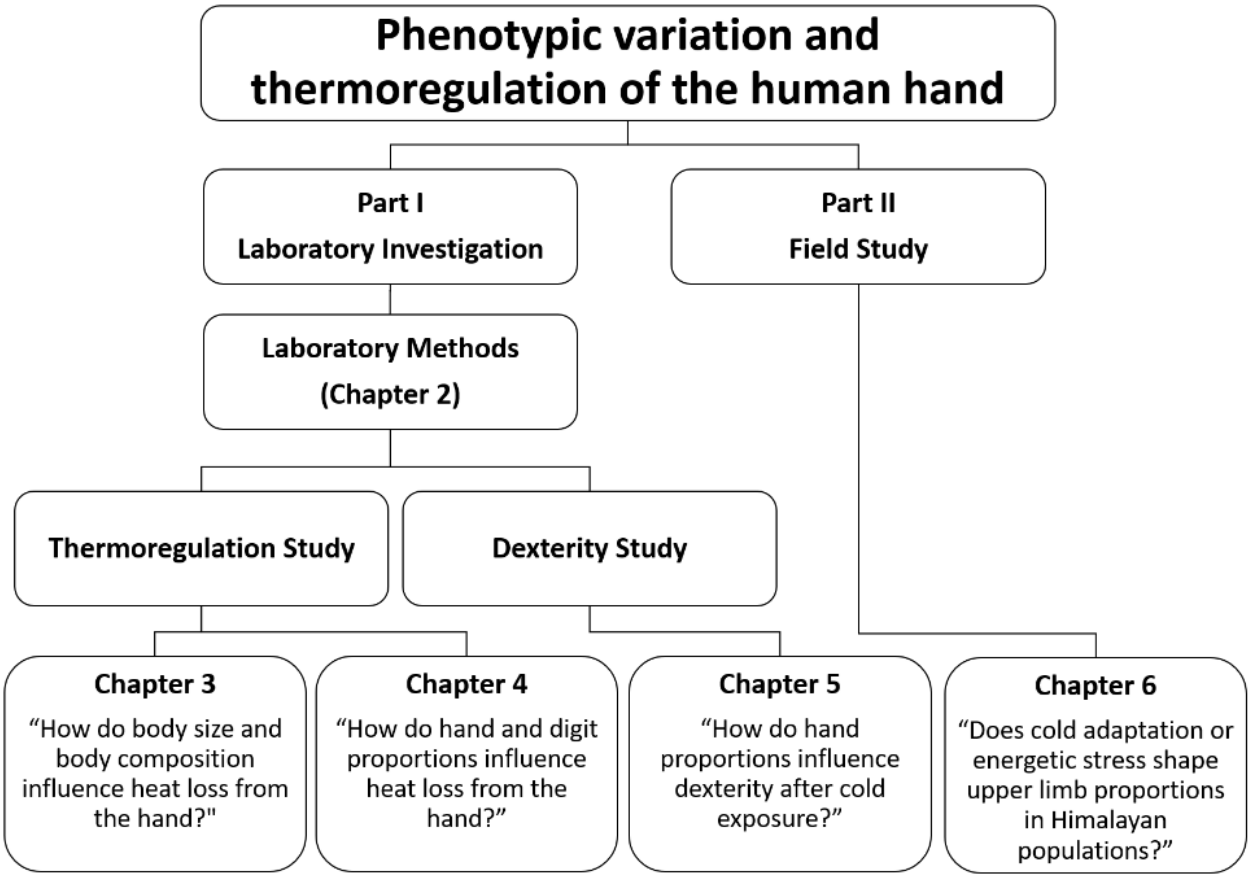


Figure 1.2 Flowchart of thesis structure and key research questions

1.5.3. Part I – Testing heat loss from the hand *in vivo*

Part I reports the findings of the laboratory investigation on heat loss from the hand and the factors that affect it *in vivo*. The methods for all the laboratory results chapters (Chapters 3-5) are collated in Chapter 2. How data from the separate studies were analysed is detailed within each individual results chapter.

Chapter 3 reports on the influence of body size and body composition on heat loss from the hands during severe cold exposure. As the body is a dynamic system with both thermogenic and insulative tissues, the relative influence of both body size and body composition on maintaining hand temperature during immersion was assessed. Thermal imaging was used to determine heat loss during a 3-minute ice-water hand immersion test carried out on 114 volunteers (female=63, male=51). Established anthropometric measures were used to quantify body size, and bioelectrical impedance analysis determined body composition through measurement of skeletal muscle mass and fat mass. This study has potential significance for understanding which individuals are more susceptible to cold injury, based on their body size and composition. The implications for our interpretation of phenotypic variation in body size and composition across populations and whether that relates to thermoregulation are also discussed.

Chapter 4 tackles the key assumption of Allen's rule, testing whether ecogeographical patterns seen in hand proportions with heat loss directly. Using the same sample as chapter 3, the influence of hand and digit dimensions on heat loss during ice-water hand immersion was evaluated. 2D and 3D scanning techniques were used to assess hand and digit dimensions. Thermal imaging analysis was used to quantify heat loss during a 3-minute ice-water immersion of the hands. This section of the study has significant implications for the applicability of Allen's rule to the hands.

Chapter 5 evaluates the relationship between hand and digit dimensions and dexterity after severe cold exposure. As wide hands are hypothesised to lose less heat than narrow hands, and narrow digits are associated with greater dexterity, this study aims to test whether wider hands or narrower digits would protect dexterity in the cold. Participants (N=40) carried out the Purdue pegboard test before and after the 3-minute ice-water hand-immersion. Their hand length, hand width, and digit lengths were measured using standard anthropometric methods. This element of the study tests whether dexterity in cold conditions reflects patterns seen at room temperatures in dexterity relating to digit proportions. This may have important implications for interpreting the morphology of both extinct and extant hominins.

1.5.4. Part II – Investigating environmental stresses and phenotypic variation in Himalayan populations

Part II comprises one chapter (Chapter 6) detailing an individual field study with its own introduction, methods, results and discussion. Chapter 6 documents a field study carried out in the Nepalese Himalayas, assessing how the multi-stress environment of high altitude manifests in phenotypic variation in the local populations. The multi-stress environment of high altitude has been associated with growth deficits in humans, particularly in zeugopod elements (forearm, lower leg). This pattern has been observed in Andeans but has yet to be tested in other high altitude populations. In Himalayan populations, other factors, such as cold stress, may shape limb proportions. This field study investigated whether relative upper limb proportions of Himalayan adults (n=254) differ between highland and lowland populations and whether cold adaptation or an energetic stress response may be acting here. Height, weight, humerus length, ulna length, hand length, and hand width were measured using standard methods. This field study is important for assessing whether cold adaptation can be seen in multi-stress environments.

Chapter 7 provides a general discussion of the results of both the laboratory and field investigations. This section discusses noteworthy elements of the study and the implications of these results for our understanding of the selection pressures on the human hand, and how thermoregulation is one of the many contributing factors to phenotypic variation in the human hand.

PART I – Laboratory Investigation

Chapter 2

Laboratory Methods

The following methods apply to results Chapters 3-5.

2.1. Ethics

Participation was voluntary and unpaid, and the study conducted according to accepted international ethical standards for research involving human subjects (Declaration of Helsinki) (World Medical Association, 2013). The study was approved by the Cambridge Human Biology Ethics Committee (HBREC.2016.022). Written informed consent was obtained from all participants (ethics approval detailed in Appendix 1).

2.2. Sample

Participants were students and residents in Cambridge, UK, and were recruited via email announcement to mailing lists of University sports societies and individual Cambridge colleges (recruitment detailed in Appendix 1). As ancestry is known to affect vasoregulation (Farnell et al., 2008; Lee et al., 2013; Maley et al., 2014; Cheung, 2015), all participants were of European origin (self-identified). Participants were excluded if they were smokers or had any conditions known to affect peripheral circulation: Type I or II diabetes, prior cold injury or hypothermia, cold-related asthma, or Raynaud's disease. As Raynaud's disease is often undiagnosed, each volunteer was asked if they regularly experienced the following symptoms in the fingers: severe cold, white or blue discolouration, numbness or "pins and needles", stinging or throbbing pain. If two or more of the symptoms were experienced, then the volunteer was excluded from the study, to minimise influence of unknown circulatory variation. All participants were right-handed, to negate any differences handedness might have on the experiment. The information relating

to handedness, health conditions, and ancestry was obtained via a screening questionnaire (see Appendix 1). Participants refrained from consuming caffeinated drinks and alcohol 12 hours before the study. Participants wore uniform garments to minimise the effect of differential clothing during the study.

2.2.1. Thermoregulatory study (Chapters 3 and 4)

A sample of 114 participants (Female=63, Male=51), aged 18-48, took part in the study at the Department of Archaeology at the University of Cambridge. Individual Cambridge colleges and sports societies were approached to obtain a sample with a range of body sizes and body compositions, including rowing, cycling, gymnastics, basketball, powerlifting, as well as relatively sedentary individuals. Several participants withdrew at certain points during the study[2]. A total of 95 participants completed every part of the study. As this study was dependent on individuals deciding to take part voluntarily, this study was based on convenience sampling, which may have caused potential bias. This would predominantly be volunteer bias; those with an interest in their own thermoregulation, body composition or other variables may be more likely to participate, which may result in data skewing. Potential bias may also result from who the investigator was able to contact. The email lists to Cambridge colleges and sports societies may not be

[2] Five participants (two women, three men) withdrew after 6 minutes of post-immersion monitoring due to discomfort. Two participants (both female) chose not carry out body composition analysis for personal reasons. One participant (female) did not have any hand measurements taken due to an electrical fault on the day. Eight participants (3 women, 5 men) chose to not undergo 3D hand scanning for health purposes as it involved flashing lights from the scanner.

representative of the entire Cambridge community, particularly as most volunteers were from sports societies, and thus the body types and fitness of participants may not be representative of the broader community.

2.2.2. Dexterity Study (Chapter 5)

A separate sample of 40 participants (Female=25, Male=15), aged 19-47, took part in the study. Students and staff of the University of Cambridge were asked to participate via email through individual college mailing lists. Whilst age is known to affect dexterity (Carmeli et al., 2003), this effect is only considered significant on average beyond the age of 65 (Dayanidhi and Valero-Cuevas, 2014); as participants were below the age of 65, they were not separated into age groups. Participants with a relatively sedentary lifestyle and without notably dextrous hobbies (such as piano-playing, sewing) were chosen to ensure that participants did not have significantly different dexterity experience. As this study was dependent on individuals deciding to take part voluntarily, this study was based on convenience sampling, which may have caused potential bias, as in the thermoregulatory study (Chapters 3 and 4). However, this study recruited participants from college mailing lists only, and thus was less likely to have a bias towards individuals actively partaking in sport.

2.3. Anthropometry

2.3.1. Whole-body anthropometry (Chapters 3-5)

Height was measured unshod to the nearest 0.1cm using a SECA-274 stadiometer (SECA Ltd, Birmingham, UK). Weight, fat mass, and skeletal muscle mass were measured to the nearest 0.1 kg using a SECA mBCA-515 segmental body composition analyser (SECA Ltd, Birmingham, UK), which uses bioelectrical impedance. Skeletal muscle mass here is defined as all muscle mass in the body, excluding smooth muscle mass, and is calculated

using a standardised algorithm from the bioelectrical impedance scores (Bosy-Westphal et al., 2008, 2017). Relative fat mass and relative skeletal muscle mass were calculated as a percentage of total body weight.

2.3.2. Hand anthropometry (Chapters 4 and 5)

Two 2-dimensional scans were taken of the left hand with palm facing downwards with uniform pressure on the scanner, the first image with digits spread as wide as possible (Figure 2.1A), the second with fingers together (Figure 2.1B), using a Canoscan Lide 600F (Canon Ltd, UK). The left hand, which was nondominant in this study as all participants were right-handed, was chosen because vasculature and vasoregulation is known to vary to a greater degree in the dominant hand (Kleinert et al., 1989). Each scan was processed using ImageJ image processing software. In the thermoregulatory study (Chapters 3 and 4), the first and third digit lengths and widths, hand length and hand width were measured to the nearest mm. The third digit was chosen for investigation as it is the longest digit, the distal end of which forms the terminal landmark of the hand length measurement (Figure 2.1), and so can provide a direct ratio with palm length. The first digit was also chosen for investigation, as it develops via a different sequence of *Hoxd* gene expression in comparison to the other digits (Montavon et al., 2008), and thus has greater potential to have significantly different proportions. In the dexterity investigation (Chapter 5), the second digit was also measured as the second and first digit are essential for creating the precision pinch grips unique to human dexterity (Kivell et al., 2016). Measurements from 2-dimensional scans yield slightly lower values than traditional anthropometric methods (Manning et al., 2005), but this error is minimal, with photocopies yielding an average of 0.31mm greater digit length than when measuring directly from the hand for digits 2-5. The photocopy method enabled significant time-saving for participants and allowed for repeatability of measurements for intra-observer error tests.

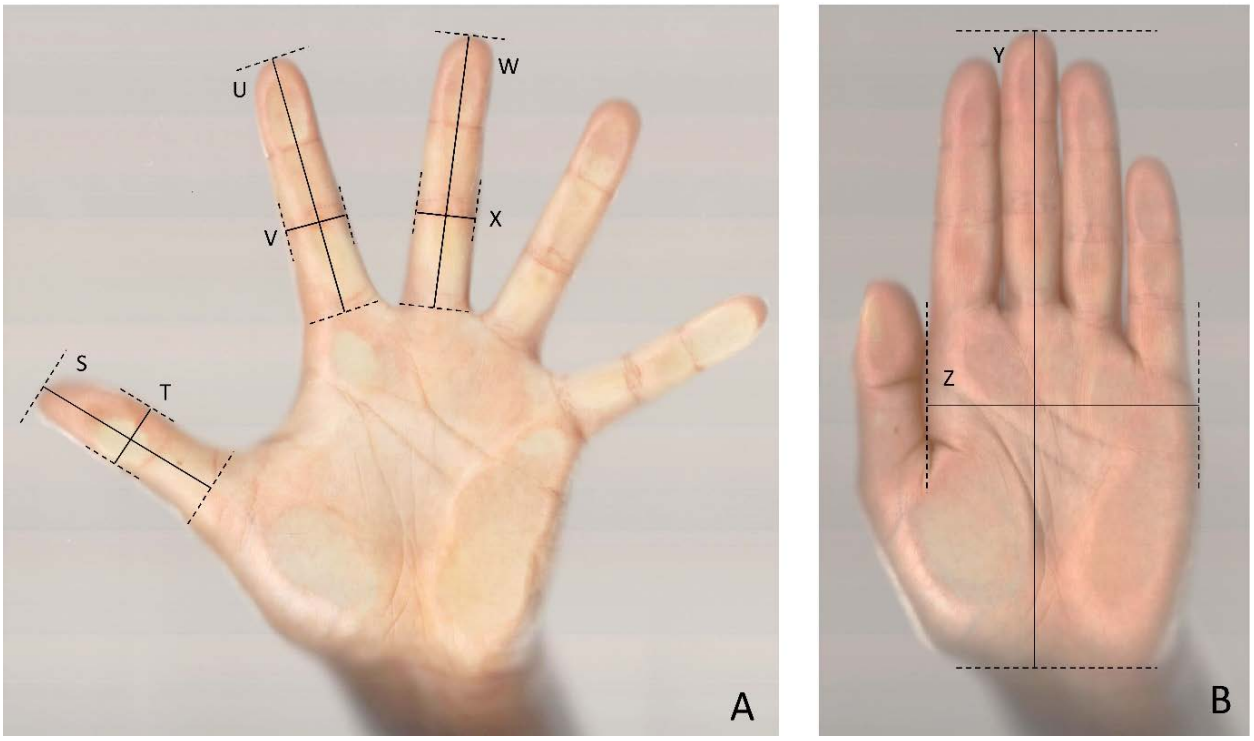


Figure 2.1 Examples of images used for hand measurements. Panel A: 2D photocopy with digits spread. S=first digit length, T= first digit width, U=2nd digit length, V=2nd digit width, W=third digit length, X=third digit width; Panel B: 2D photocopy with digits together. Y= hand length, Z=hand width.

Hand length was measured as the linear distance between the most anterior projection of the third digit to the mid-point on the wrist crease (between the proximal edge of the triquetrum and the proximal edge of the trapezium). Hand width was the linear distance between the radial side of the second metacarpophalangeal joint to the ulnar side of the fifth metacarpophalangeal joint. First digit length was measured as the linear distance between the most anterior projection of the first digit and the mid-point between the distal edge of the first metacarpophalangeal joint and the skin crease between the first and second digit. First digit width was measured as the greatest linear distance at the joint between the proximal and distal phalanges. The first metacarpophalangeal joint was not used to measure width to avoid variation in skin webbing across the joint affecting this measurement. Second and third digit lengths were measured as the linear distance between the most anterior projection of the digit and the mid-point of the

metacarpophalangeal joint. Second and third digit widths were measured as the greater linear distance at the joint between the proximal and middle phalanges.

Hand surface area and volume were measured to the nearest mm^2 and mm^3 respectively using an Artec Eva 3D scanner (Artec Ltd., USA); for the scan, the participant was seated with the left elbow resting on a bench and supported by foam padding, to prevent movement during the scan. Artec Studio software version 10.0 was then used to estimate both hand surface area and hand volume from the horizontal slice between the radial styloid process and the ulnar styloid process (Figure 2.2).

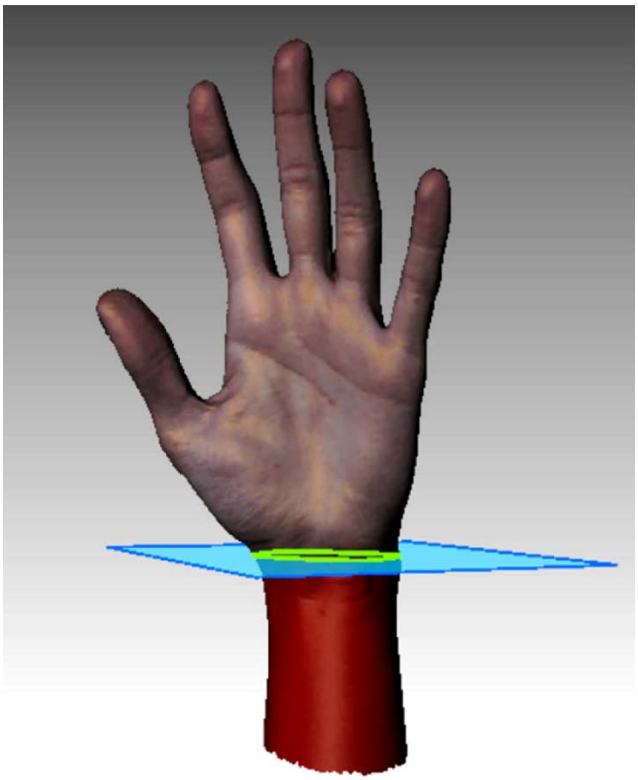


Figure 2.2 3D hand scan used to measure surface area and volume of hand

A precision test was performed to determine intra-observer error on both the 2D and 3D hand scan images. Five random images of each scan type were selected and processed on five separate days, with a minimum of 24 hours between re-measurement.

Intra-observer mean error across all measurements was 1.38mm, and thus considered to be within accepted standards for all measurements (R>0.9; rTEM<10%) (Ulijaszek and Kerr, 1999).

2.4. Experimental protocol (Chapters 3-5)

Room temperature and humidity were controlled (25˚C, 40%). After a 30-minute acclimation period where participants were seated and at rest, participants had a thermal image taken of the dorsal surface of their hands from a seated position while resting their palms on an insulated surface with fingers together. Whilst the dorsal regions of the digits may marginally differ in temperature from that of the finger pads used in the dexterity test, images of the dorsal side were taken for ease of positioning for participants. Thermal images were taken using a FLIR T460 infrared camera (FLIR Systems Inc., USA).

2.4.1. Thermoregulatory Study (Chapters 3 and 4)

In the thermoregulatory study, participants then put on non-latex surgical gloves to avoid evaporative cooling from wet skin during the rewarming period. Whilst the non-latex gloves may have acted as a thin barrier to heat loss, this effect would be small in comparison to the considerable cooling resulting from wet skin (Geng, 2001), which may have reduced reheating considerably. Participants immersed both of their hands in 0˚C ice water for three minutes. This time period was chosen as this is shorter than the onset of CIVD (Adams and Smith, 1962; Takeoka et al., 1993; Daanen and van Ruiten, 2000; Tyler et al., 2015). Both hands were immersed to avoid variation in blood flow between hands when only one is immersed, as reported by Mekjavic *et al.* (2008). Hands were immersed to the distal edge of the ulnar styloid process, which was marked with a waterproof marker on the gloves. After immersion, the gloves were removed, and hands returned to the original imaging position and a second thermal image was taken (zero minutes after

immersion). Thermal images were then taken at two-minute intervals for ten minutes. Core temperature was monitored as a safety precaution immediately before immersion and in the final minute of immersion using an infrared tympanic thermometer (Braun Thermoscan IRT 3020EE- Braun GmBH, Germany).

2.4.2. Dexterity Study (Chapter 5)

In the dexterity study, after the first thermal image was taken, participants then undertook the Purdue pegboard dexterity test (Figure 2.3A). This is an established dexterity test which is widely used in clinical and physiological studies (Daanen, 2009). The assembly version of the test was used in this study, which tests the ability to assemble washers and pins using fine finger dexterity in both hands (Figure 2.3B & C)(Parkway and Box, 2002; Gallus and Mathiowetz, 2003; Yancosek and Howell, 2009). The assembly test was chosen for several reasons: its ability to measure the completion of thumb-finger precision pinch grips in quick succession, which may be required for certain survival tasks such as threading, sewing, delicate preparation of food, treating small wounds (Fleishman and Ellison, 1962; Marzke, 1997); its ease of repeatability; its comparability to other studies (Gallus and Mathiowetz, 2003; Daanen, 2009), and the likelihood of producing a significant range in dexterity values. Whilst other tests carried out on the Purdue pegboard last only 30 seconds, which is often insufficient to distinguish any differences in dexterity within or between individuals, the assembly test is carried out over 60 seconds, increasing the time period for which dextrous abilities can be established. In the assembly test, the aim was to build as many assemblages of a specific pin-washer-collar-washer configuration in one minute, timed by a stop watch. Any digits from either hand could be used to make each assemblage. Assemblages had to be completed one at a time.

A)

B)

C)

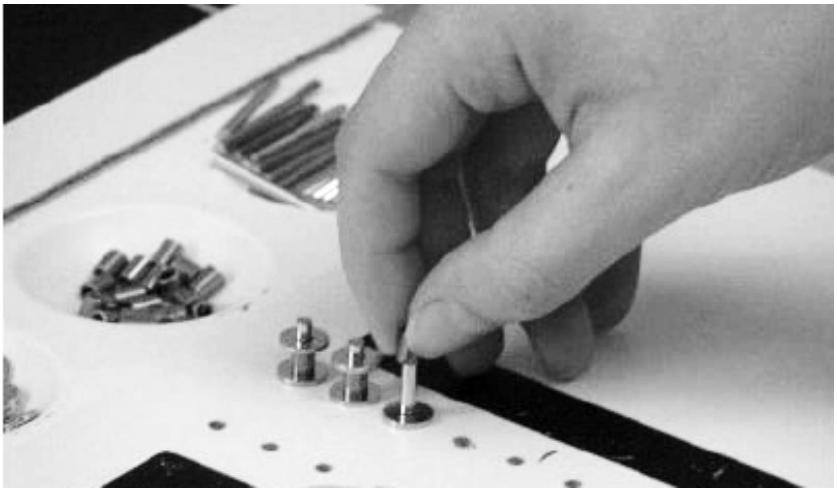


Figure 2.3 A) Image of a Purdue Pegboard B) Image of pins, collars, and washers C) Image of Purdue pegboard Assembly test

An assemblage was made by placing a pin in any hole of the pegboard, followed by placing a washer over the pin, a collar over the pin, and another washer other the pin. After one minute, the n mber of pins,washers, and collars placed in correct positions were totalled to give a score representative of fine finger dexterity using both hands. Each participant was given three practice runs to familiarise themselves with the dexterity task, before carrying out the official pre-immersion test, after which a second thermal image was taken.

Then the participants carried out the immersion stage of the experiment. As with the thermoregulatory investigation, participants put on non-latex surgical gloves and then immersed their hands in 0˚C ice water for 3 minutes. Core temperature was monitored as a safety precaution immediately before immersion and in the final minute of immersion using an infrared tympanic thermometer (Braun Thermoscan IRT 3020EE- Braun GmBH, Germany). After immersion, the gloves were removed, and a third thermal image was taken immediately (zero minutes after immersion). The participant then repeated the dexterity test to measure post-immersion dexterity, and then a final thermal image was taken.

2.5. Thermal image analysis (Chapters 3-5)

Thermal images were analysed using FLIR Tools+ software (FLIR Systems Inc., USA). For each thermal image, the average temperature of each digit from the cuticle base to the metacarpophalangeal joint was measured, and then temperature was averaged over the five digits of the left hand to produce average digit temperature at each time point (Figure 2.4). Digit temperature was averaged across the length of the finger because the nail bed was the landmark most consistently and reliably identifiable on thermal images.

Though blood supply differs along the length of the finger (Ikeda et al., 1988; Rodriguez-Niedenfuhr et al., 2001), this approach was used to enhance reliability of landmark location on the digits. All temperatures were measured to the nearest 0.01˚C. A precision test was performed to determine intra-observer error on thermal image analysis. Five random images were selected and processed on five separate days, with a minimum of 24 hours between re-measurement. Intra-observer mean error across all measurements was 0.24˚C, was determined to be within accepted standards for all measurements (R > 0.9; rTEM < 1%) (Ulijaszek and Kerr, 1999).

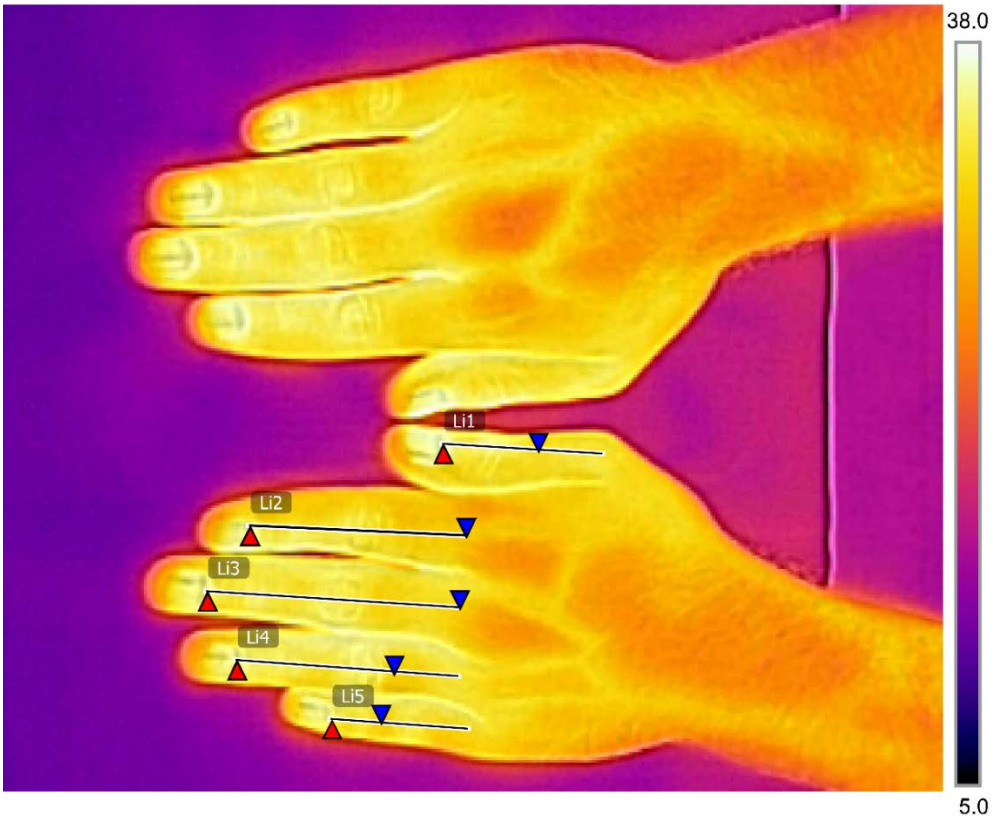


Figure 2.4 Example of Thermal Image Analysis. Li=Line; Red triangle= Highest temperature point on the line; Blue triangle= Lowest temperature point on the line

Chapter 3

Body size and body composition effects on heat loss from the hands during severe cold exposure

This chapter was published online in the American Journal of Physical Anthropology on 11 February 2018 (Payne et al., 2018a). An expanded literature review has been added for the purpose of completeness in this thesis.

Objectives: This study investigated the influence of body size and composition on maintaining hand temperature during severe cold exposure. The hand's high surface area-to-volume ratio predisposes the hand to heat loss, increasing the risk of cold injury and even hypothermia, which are major selective pressures in cold environments. Whilst vasoregulation may reduce heat loss from the hand, the effect of body form, tissue thermogenesis, and body insulation on heat loss is unknown.

Materials and Methods: Thermal imaging was used to determine heat loss during a three-minute ice-water hand immersion test carried out on 114 volunteers (Female=63, Male=51). Established anthropometric measures were used to quantify body size, and bioelectrical impedance analysis determined skeletal muscle mass and fat mass.

Results: Skeletal muscle mass relative to weight was a highly significant predictor of heat loss, while fat mass, height, and weight were not. Body composition and body size had little to no significant influence during rewarming after immersion.

Discussion: The thermogenic properties of muscle mass support maintenance of hand temperature during severe cold exposure. The findings here suggest that muscular

individuals are less susceptible to heat loss and cold injury, and may be better at manual tasks in cold conditions than non-muscular individuals.

3.1. Introduction

Population dispersals to regions of high latitude and altitude exposed humans to significant cold stress (Wells and Stock, 2007). To reduce the risk of death by hypothermia or cold injury, a range of thermoregulatory traits have developed to generate heat or minimise heat loss in cold environments (Parsons, 2014): shivering and non-shivering thermogenesis, increased basal metabolic rate, and dynamic vasomotor control. Furthermore, the development of clothing would have enabled expansion into even colder climates (Gilligan, 2010). Despite the body being protected from the cold, the hands would have remained exposed during manual tasks essential for survival (Heus et al., 1995), and thus the hands would still be at risk of cold injury. The hands have a large surface area-to-volume ratio, which is beneficial for radiation, but potentially challenging to maintaining thermal balance in cold conditions (Savage and Brengelmann, 1996). Whilst dynamic vasomotor control in the hand would be essential in cold conditions, the thermodynamic properties of the body are likely to influence extremity temperature and dexterity, but this relationship has yet to be explored. The current study investigates the influence of body size and body composition on heat loss and rewarming in the hand, to determine whether they affect hand temperature and dexterity in cold conditions.

In cold environments, the high surface area-to-volume ratio of the hand potentially puts the hand at risk of excess heat loss, which may lead to cold injury, and a wasteful loss of valuable body heat. A direct relationship between hand size and core body temperature has been observed in Peruvian Quechua (Weitz, 1969), demonstrating the hand surface area-to-volume ratio may associate with whole-body thermoregulation. Whilst it is difficult to determine whether heat loss from the hand would occur to the extent of causing whole-

body thermal imbalance and potentially fatal hypothermia, the hands to indeed have vasoregulatory mechanisms to reduce heat loss from the hands, indicating that such mechanisms do indeed have some benefit to our survival. (Taylor, 2014). These dynamic vasomotor responses include vasoconstriction and CIVD (Lewis, 1930; Cheung, 2015). In groups living in cold regions, vasomotor responses are amplified in one way or another depending on the response, as summarised by Frisancho (1993). Either vasoconstriction occurs to a greater degree, as seen in high altitude-dwelling Himalayan groups (Takeoka et al., 1993), or the CIVD response has a greater pulse amplitude, as seen in highland Peruvians (Little and Hanna, 1977), and high latitude-dwelling Inuit and Athapascan groups (Brown et al., 1953; Page and Brown, 1953; Meehan, 1955; Elsner et al., 1960; Miller and Irving, 1962; Steegmann, 1977). Increasing evidence suggests that variation across the globe in vasomotor responses appear to result from differences in acclimatisation (Cheung and Daanen, 2012); for instance, no differences were found in vasomotor responses between Artic natives and those of tropical origin after daily exposure to cold over a period of 7 weeks (Purkayastha et al., 1992). Developmental acclimatisation is also thought to occur, indicated by cross-sectional studies demonstrating increased CIVD amplitude with age (Little, 1976; Little and Hanna, 1977). Whilst acclimatisation appears to be essential in generating nuanced vasoregulatory responses to environmental temperature, there is also evidence to suggest that genetics may have a small influence on vasomotor responses, as indicated by differences in CIVD peak temperatures in UK-born residents of different ethnic origins (Maley et al., 2014). Whilst the extent of influence of genetics and acclimatisation on variation in vasoregulatory adaptations requires further clarification, it is evident that we have indeed developed effective vasomotor responses to deal with severe cold.

While dynamic vasoregulation in the hands is relatively well understood, the role of other factors in heat flux from the hand remains under-studied. Heat loss is also influenced by the insulative and thermogenic properties of different tissues (Fournet et al., 2013; Marins et al., 2014). Fat mass has traditionally been considered the body's predominant insulative tissue under cold stress, as populations exposed to cold stress are found to have a higher percentage fat mass, relative to populations from tropical or temperate climates (Shephard et al., 1973; Houghton, 1990; Jones and White, 1994; Craig et al., 2001; Piers et al., 2003). Subcutaneous fat mass has also been considered the dominant insulating tissue in whole-body immersion investigations (Sloan and Keatinge, 1973; Toner and McArdle, 1988; Glickman-Weiss et al., 1996). This is consistent with investigations demonstrating that adipose tissue has approximately double the thermal resistance of skeletal muscle (Hatfield and Pugh, 1951; Valvano et al., 1984). Whole-body immersion investigations have also indicated that muscularity does not protect from heat loss (Oksa et al., 2007), although the extent of blood-perfusion in the muscle does probably play a role (Veicsteinas et al., 1982; Xu et al., 2007). Though considered important for insulation, white adipose tissue has been shown to have limited thermogenic capacity (Granneman et al., 2003; Seale et al., 2011). Thermogenesis in white adipose tissue results from promoting the expression of the uncoupling protein which is involved in brown adipose tissue non-shivering thermogenesis (Nedergaard and Cannon, 2014). Uncoupling refers to mitochondrial respiration without ATP synthesis, where energy is released as heat within the brown adipose tissue in non-shivering thermogenesis (Rousset et al., 2004). When activated, as little as 50g of brown adipose tissue can contribute up to 20% of energy expenditure (Rothwell and Stock, 1983). The presence of brown adipose tissue has been detected in some adults of cold climate populations, but the extent to which it is found throughout populations globally has yet to be established (Nedergaard et al., 2007; Cypess et al., 2009). Whether the insulative and

thermogenic properties of adipose tissue significantly influence heat loss from the extremities is currently unknown.

Alongside adipose tissue, skeletal muscle mass is also likely to play a role in thermoregulation. In adults, skeletal muscle mass is a key thermogenic tissue (Rowland et al., 2015; Pant et al., 2016), and has been associated with maintenance of core temperature during whole-body cooling (McArdle et al., 1984b). When exposed to cold environmental temperatures, active non-shivering thermogenesis in skeletal muscle is triggered, which has been linked to calcium ion cycling (Block, 1994; Rowland et al., 2015). Shivering thermogenesis may also be activated below a certain threshold environmental temperature, whereby muscle contraction results in thermogenesis (Block, 1994). Indeed, indigenous Arctic and high altitude populations have higher muscle masses than populations from temperate lowland regions (Picon-Reategui and Picón-Reátegui, 1961; Ducros and Ducros, 1979; Gnaiger et al., 2015), indicating the importance of skeletal muscle mass in the maintenance of body temperature under cold stress, although this may also result from differences in activity. Even when the body is not subjected to cold conditions, skeletal muscle generates approximately 20-30% of total body heat at rest (Brozek and Grande, 1955; Elia, 1991; Sparti et al., 1997). Thus, due to its passive and active thermogenic properties, skeletal muscle mass plays an important role in thermoregulation. However, the influence of relative fat and skeletal muscle masses on heat loss from the extremities has yet to be explored.

When examining heat loss from the extremities, body size may also be an important influence. Increased body size has generally been associated with colder climates (Bergmann, 1847; Beall and Goldstein, 1992; Ruff, 1994; Katzmarzyk and Leonard, 1998; Gustafsson and Lindenfors, 2009; Hancock et al., 2011; Temple and Matsumura, 2011; Foster and Collard, 2013; Gilligan et al., 2013; Hadley and Hruschka, 2014; Roseman and

Auerbach, 2015; Savell et al., 2016). This association is considered to be a cold adaptation, whereby populations inhabiting cold climates tend to have larger bodies, with a smaller surface area-to-volume ratio, which will lose less heat per unit volume to the surroundings than smaller bodies (Bergmann, 1847; Ruff, 1994). During thermal stress, body size and core temperature do indeed show a direct positive relationship (Burton and Edholm, 1955; Pugh and Edholm, 1955; Folk, 1974; Shapiro et al., 1980; LeBlanc, 1988; Frisancho, 1993; Havenith, 2001). This relationship will result in body size affecting heat flux in the extremities (Havenith, 2001; Daanen, 2003; Chudecka, 2013), due to the dynamic nature of the whole-body system. During cold stress, however, the activation of physiological mechanisms, including thermogenesis and vasoregulation, mean that the model of heat loss from the body is unlikely to follow a simple surface area-to-volume ratio rule (Steegmann, 2007).

The role of body size and body composition on human cold adaptation still requires further investigation (Steegmann, 2007). Observing variation in heat loss will directly test the assumptions used to support cold adaptation theory. This research seeks to determine whether body size and body composition have any effect on heat loss from the hand, or whether this is countered by dynamic vasoregulation. As both body size and body composition are, on average, different between the sexes, the potential difference in heat loss capacities (McArdle et al., 1984a; b), and heat loss from the extremities between the sexes (Jay and Havenith, 2004), should also be investigated. The current study set out to test the following questions during an ice-water hand immersion experiment: do individuals with a larger body size lose less heat from the hands than those with smaller body size; do individuals with more muscle mass or more fat mass lose less heat from the hands: do women lose more heat from the hands than men; does weight, muscle mass, fat mass or sex affect rewarming?

3.2. Methods

All methods are detailed in Chapter 2. Sampling can be found in section 2.2; anthropometry can be found in section 2.3.1; experimental protocol can be found in section 2.4.1; thermal image analysis can be found in section 2.5.

3.2.1. Statistical analysis

All continuous variables were assessed for normality using the Shapiro-Wilk Test. Paired *t*-tests were used to test for differences in pre-immersion core temperature and core temperature during the final minute of immersion. Average digit temperature immediately after immersion (T_{Post}) was calculated as a percentage of average digit pre-immersion temperature (T_{Pre}), to remove any influence of inter-subject variation in T_{Pre}. Average digit temperature at the proceeding time points (two (T_2), four (T_4), six (T_6), eight (T_8), and ten (T_{10}) minutes after immersion) was also calculated as percentages of T_{Pre}.

Sex differences in body size and composition variables, average digit temperature at each time point, and change in average digit temperature at every time interval were assessed using independent-sample *t*-tests.

Spearman's rank correlation analysis was used to determine whether any body variables correlated significantly with T_{Post}, T_2, T_4, T_6, T_8, or T_{10}. A Bonferroni correction factor was applied to allow for multiple comparisons using different body size and body composition variables. Bivariate Pearson's correlation analysis was used to assess relationships between skeletal muscle mass and fat mass.

Stepwise regression analysis was carried out to determine whether height, weight, fat mass, skeletal muscle mass, relative skeletal and muscle mass (as a percentage of total body weight, respectively) were suitable predictors of T_{Post}, according to the following models:

Model 1

$T_{Post} = \beta_0 + \beta_1$[Height] + β_2 [Weight] + β_3 [Skeletal Muscle Mass] + β_4 [Fat Mass]

Model 2

$T_{Post} = \beta_0 + \beta_1$[Relative Skeletal Muscle Mass] + β_2 [Relative Fat Mass]

The models were applied to the sample both when sexes were pooled and separated. All variables in the regressions were assessed for normality using regression residual plots. To determine whether there were any additional sex effects beyond body size or body composition variables, the standardised residuals of any significant models were tested for significant differences between the sexes using independent *t*-tests. All statistical analysis was carried out using SPSS 25.0 for Windows.

3.3. Results

3.3.1. Test sample statistics

Table 3.1 summarises the body size and composition variables for the test sample. Within sexes, all variables except age were normally distributed. When sexes were pooled, height, weight, relative fat mass, and relative skeletal muscle mass were normally distributed, but absolute fat mass and absolute skeletal muscle mass were not.

All body size and composition variables were significantly different between men and women. Men were significantly taller and heavier than women ($p<0.01$ for both) and had significantly greater absolute and relative skeletal muscle mass than women ($p<0.01$ for both), while women had significantly greater absolute and relative fat mass than men ($p<0.01$ for both).

Table 3.1 Summary statistics of test sample variables

	Sex	N	Minimum	Maximum	Mean (SD)
Age (years)	F	63	18	44	26 (±6)
	M	51	19	48	25 (±6)
Height (cm)	F	63	150.1	189.9	169.7 (±7.3)
	M	51	166.5	200.0	181.9 (±6.8)
Weight (kg)	F	63	41.00	88.85	63.62 (±9.46)
	M	51	60.40	118.00	78.31 (±7.64)
Absolute Fat Mass (kg)	F	62	6.21	34.43	17.29 (±5.99)
	M	51	3.10	24.56	11.92 (±4.77)
Relative Fat Mass (%)	F	62	10.50	38.70	26.41 (±6.14)
	M	51	6.60	27.30	15.21 (±5.03)
Absolute Skeletal Muscle Mass (kg)	F	62	13.70	28.80	21.43 (±2.78)
	M	51	25.40	40.00	32.87 (±3.48)
Relative Skeletal Muscle Mass (%)	F	61	28.96	41.29	33.73 (±2.72)
	M	51	36.48	48.75	42.03 (±2.66)

SD: Standard Deviation

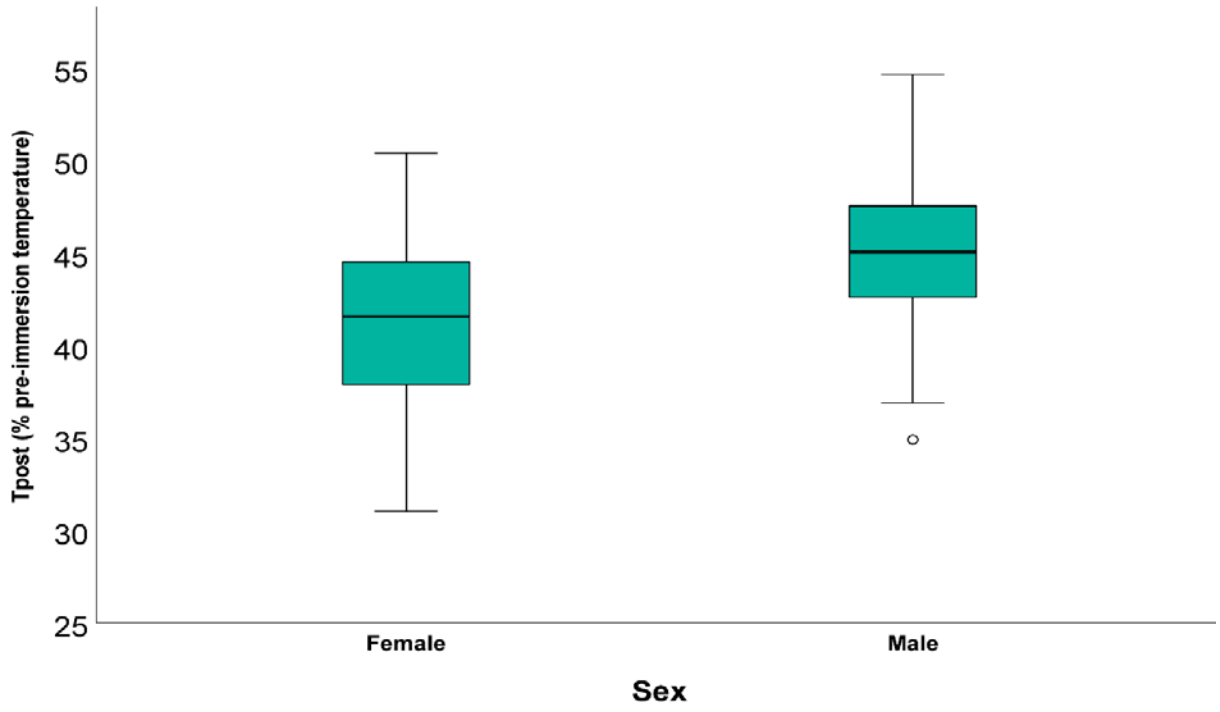


Figure 3.1 Tukey's Boxplot showing difference between men and women in TPost; each box represents the respective interquartile range (IQR), whiskers represent the lowest value still found within 1.5 IQR of the lower and upper quartiles.

3.3.2. Heat Loss

There was no significant difference in core body temperature before immersion (36.76˚C, ±0.96) and in the final minute of immersion (36.83˚C, ±0.35) (t_{113}=0.820, p>0.05). Women had significantly lower mean T_{Post} (41±5%) than men (45±4%; p<0.01, see Figure 3.1). However, men and women did not differ significantly in average digit temperature at any time point after $T_{Post.}$

The range of average digit temperatures during rewarming is shown in Figure 3.2. At the final time point, 64 participants had an average digit temperature greater than their pre-immersion temperature.

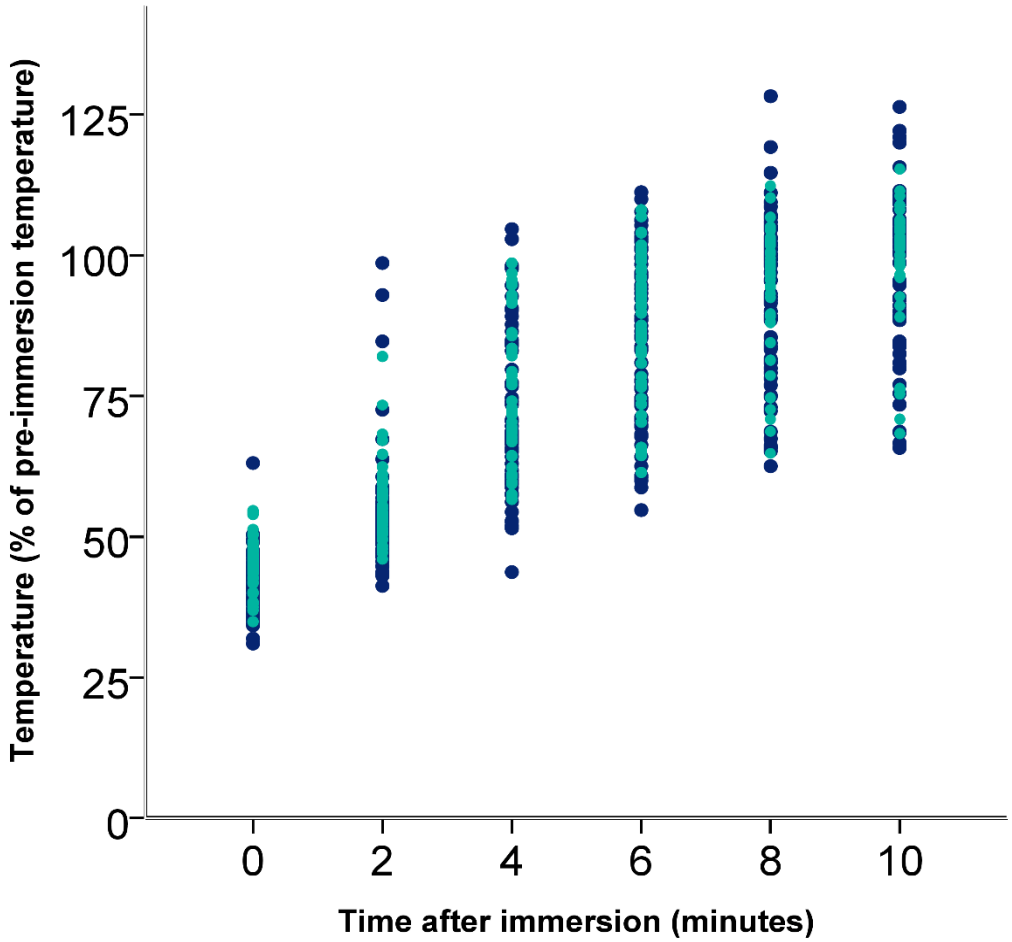


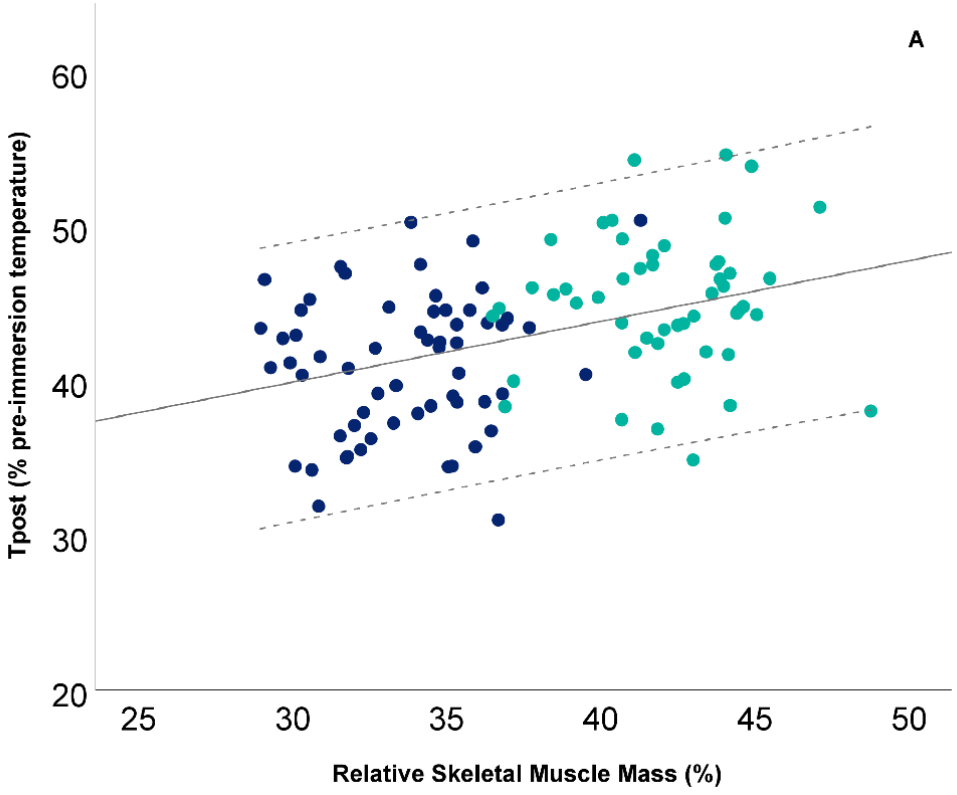
Figure 3.2 Range of average digit temperatures at each time point during the rewarming period. Blue dots: female; green dots: male

The results of Spearman's rank correlation analyses with a Bonferroni correction demonstrated that body composition variables did associate with temperature after immersion (Table 3.2). Height, weight, and absolute fat mass did not correlate with average digit temperature at any time point. When controlling for weight, relative muscle mass exhibited significant positive correlations with T_{Post} (Figure 3.3A) and T_2, while relative fat mass significantly negatively correlated with T_{Post} (Figure 3.3B). It was noted that relative skeletal muscle mass and relative fat mass significantly negatively correlated with each other (Figure 3.3C). No body size or composition variables were significantly correlated with T_4 through T_{10}.

Table 3.2 Summary of Spearman's Rank Correlation Analysis between body size and composition variables and average digit temperature during the experiment

		Average digit temperature (% of pre-immersion temperature) at given time point after immersion					
		0 mins (T_{Post})	**2 mins (T_2)**	**4 mins (T_4)**	**6 mins (T_6)**	**8 mins (T_8)**	**10 mins (T_{10})**
Height	**CC**	.282	.251	.058	.019	.048	.027
	Sig. (2-tailed)	.002	.007	.540	.839	.619	.784
Weight	**CC**	.278	.254	.110	.083	.090	.026
	Sig. (2-tailed)	.003	.007	.248	.380	.352	.793
Absolute Fat Mass	**CC**	-.233	-.129	-.026	-.025	-.044	-.048
	Sig. (2-tailed)	.014	.176	.783	.795	.650	.624
Absolute Skeletal Muscle Mass	**CC**	.390*	.320*	.133	.089	.091	.045
	Sig. (2-tailed)	.001	.001	.163	.354	.355	.650
Relative Fat Mass	**CC**	-.370*	-.224	-.053	-.050	-.049	-.034
	Sig. (2-tailed)	.001	.018	.581	.603	.618	.731
Relative Skeletal Muscle Mass	**CC**	.379*	.286	.121	.101	.083	.050
	Sig. (2-tailed)	.001	.002	.206	.294	.398	.612

*CC= Correlation Coefficient; *= significant with Bonferroni adjusted p-value (p<0.0014)*


A
Tpost (% pre-immersion temperature)
60
50
40
30
20
25
30
35
40
45
50
Relative Skeletal Muscle Mass (%)

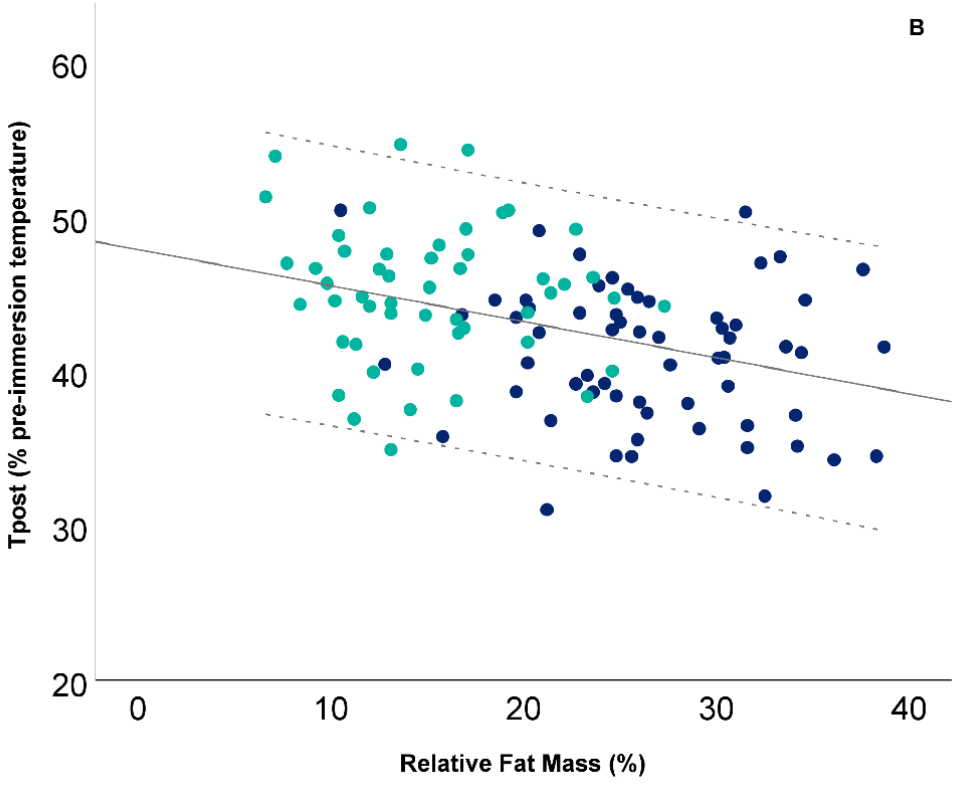

B
Tpost (% pre-immersion temperature)
60
50
40
30
20
0
10
20
30
40
Relative Fat Mass (%)

Figure 3.3.

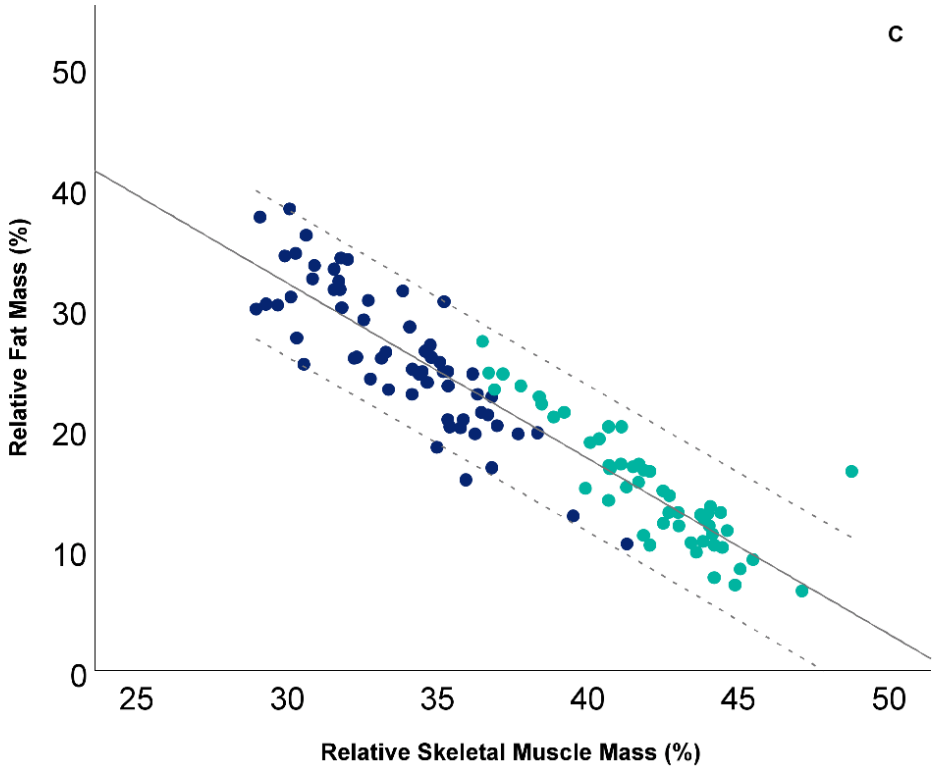


*Figure 3.3 Scatterplots of the relationship between heat loss and body composition variables, depicting a line of best fit and 95% confidence intervals. A) TPost and relative skeletal muscle mass (regression line: y=28.12+0.39*x), B) TPost and relative fat mass (regression line: y=47.81-0.23*x), and C) Relative skeletal muscle and fat masses (r=-0.922, p<0.01); blue dots: female; green dots: male*

The stepwise regression analyses determined which of the body composition variables were likely to be driving the relationships seen in the Spearman's rank correlation analyses. Absolute and relative skeletal muscle masses were both highly significant predictors of heat loss from the digits upon cold water immersion. In model 1, absolute skeletal muscle mass was the only significant predictor of T_{Post} (Table 3.3), while weight, height, and fat mass were not significant predictors of heat loss. In model 2, relative skeletal muscle mass alone was found to predict T_{Post}; relative fat mass was not a significant predictor of T_{Post}. When the sexes were analysed separately, there were no associations between any of the body size or body composition variables and T_{Post} ($p>0.05$ for both models). In the analysis of the standardised residuals of both models 1 and 2, there was no

significant difference between the sexes (p>0.05), indicating that there were no additional sex effects beyond differences in skeletal muscle mass.

Table 3.3 Summary of two stepwise linear regression models predicting TPost

Model	Predictors	B	Std. Error	β	F	P value	R^2
1	**(Constant)**	35.085	1.801			<.01	
	Absolute Skeletal Muscle Mass	.291	.066	.390	19.694	<.01	0.152*
2	**(Constant)**	28.123	1.292			<.01	
	Relative Skeletal Muscle Mass	.393	.086	.398	20.752	<.01	0.159*

*Std. Error = Standard Error; *= highly significant (p<0.01) Model 1: Excluded variables were height, weight, absolute fat mass; Model 2: Excluded variables were relative fat mass*

3.4. Discussion

3.4.1. Outcomes relating to body composition and body size

The current study showed that in healthy men and women both absolute and relative skeletal muscle mass were significant predictors of heat loss during ice-water immersion of the hand, thus demonstrating the role of body composition in thermoregulation in cold environments. Body composition and body size had little to no significant influence during rewarming after immersion at most time points, indicating that dynamic thermoregulatory mechanisms control hand temperature during rewarming. These findings demonstrate that while body composition is influential in maintaining peripheral temperatures under cold stress, the body has powerful mechanisms to reduce heat loss from the hands after brief, severe cold exposure.

Individuals with greater absolute and relative skeletal muscle mass had a higher post-immersion average digit temperature relative to pre-immersion temperature. This finding may relate to the greater thermogenic capacity of skeletal muscle relative to other tissues (Rowland et al., 2015). Greater relative skeletal muscle mass increases thermogenesis per kilogram of total weight, and thus for a given rate of heat loss, a greater amount of body heat will be replaced (Steegmann, 2007). From an evolutionary

perspective, the importance of muscle mass in reducing heat loss may explain why individuals inhabiting regions of extreme minimum temperatures tend to have greater overall muscle mass than those inhabiting tropical or temperate climes (Ducros and Ducros, 1979; Wells, 2012). Greater muscle mass may allow these individuals to better maintain the temperature of both body and extremities (Dusek, 1957; Clark and Cohen, 1960; Provins and Clarke, 1960; Provins and Morton, 1960; Havenith et al., 1995; Heus et al., 1995). In conjunction with greater muscle mass, higher metabolic rates would be required to enable this greater thermogenic capacity, and this is indeed reported in several cold-adapted populations, including circumpolar groups (Rennie et al., 1962; Leonard et al., 2002, 2005; Snodgrass et al., 2005; Brychta and Chen, 2017), and high altitude populations (Little et al., 1971; Little, 1976). Together this work shows that the ability to deliver heat effectively to peripheral tissues is driven more by metabolic capacity, such as greater muscle and metabolic rate, rather than insulation. In the context of human adaptation, even after the invention of clothing (Gilligan, 2010), human hands are still likely to have been exposed when carrying out manual tasks, and thus, having substantial thermogenic tissue, in the form of muscle mass, would have been advantageous for replacing heat lost through the extremities.

The regression models in the current study demonstrate that both absolute and relative skeletal muscle mass are highly significant predictors of hand temperature after ice water immersion. Whilst these predictors have a relatively small effect, this is generally to be expected when observing a variable such as temperature, which is influenced by multiple factors. Furthermore, vasoregulation will have a significant influence on hand temperature during cold stress, irrespective of body size or body composition, as vasoregulatory responses are known to vary significantly (Cheung, 2015). As discussed, there are heterogeneous vasoregulatory responses in populations residing in different cold

regions (Brown et al., 1953; Little and Hanna, 1977; Frisancho, 1993). Indeed, despite the known powerful vasoregulatory mechanisms, the current study still found body composition effects on hand temperature during cold stress, indicating the importance of body composition in thermoregulation.

Absolute and relative fat mass did not significantly predict heat loss. Although fat mass is traditionally considered an insulating tissue (Henriques and Moritz, 1947; Lipkin and Hardy, 1954), it did not have a significant effect on heat loss or rewarming. This may be because relatively little fat mass is found in the hands (Taylor, 2014), and therefore the hands are poorly insulated, leaving them susceptible to heat loss. Interestingly, relative fat mass negatively correlated with T_{Post} (Table 3.2). However, given the significant negative correlation between relative skeletal muscle mass and relative fat mass, this result may be related more to muscle tissue than to any direct biological link between body fat mass and heat loss from the hand. The significant correlation between body tissues often makes it difficult to partition their effects during cold exposure, as demonstrated by reanalysis of Sloan and Keatinge's (1973) whole-body immersion investigations (Steegmann, 2007).

There were no significant predictors of T_{Post} when the sexes were analysed separately. There may not have been sufficient variation within the sexes in body size and body composition for a relationship to be apparent. Skeletal muscle mass and fat mass are closely associated with sex, thus again making it difficult to partition the effects of sex and different body tissues. On analysis of the residuals from Model 2, no significant difference was found between the sexes, demonstrating that, once relative skeletal muscle mass is taken into account, there are no additional sex effects. This finding aligns with previous hand heat loss investigations carried out by Jay and Havenith (2004), where no significant difference was found between the sexes when body size was taken into account. Further research using an even wider range of body types and body compositions within each sex

may shed further light on the influence of sex versus body composition of heat loss from the hands.

3.4.2. Rewarming patterns

No body size or composition variables correlated with T_4, T_6, T_8, and T_{10} suggesting that other factors influence rewarming here, such as hand size, or vasoregulation. As relative skeletal muscle mass influences average digit temperature up to two minutes after immersion, but no longer has an effect at four minutes, this indicates that other factors such as vasodilatation may have a greater influence on digit temperature from this time point onwards. This agrees with previous findings that the time for rewarming vasodilatation to occur varies greatly between individuals; several studies have found an average of two to three minutes post-immersion lag time before seeing a significant vasodilatory-induced change in finger temperature (Adams and Smith, 1962; Itoh et al., 1970). Furthermore, hand volume has been shown to influence rewarming (Jay and Havenith, 2004), which was assessed separately (see Chapter 4).

3.4.3. Exceeding baseline temperature

The current study demonstrated that average digit temperature can exceed pre-immersion temperature after a 10-minute rewarming period. This is not commonly reported in immersion tests (Elsner et al., 1960; Krog et al., 1960; Mathew et al., 1979; Bergersen et al., 1999; Daanen et al., 2007; Mekjavic et al., 2008; Cheung, 2015), which may be due to a difference in protocol (Silverthorn and Michael, 2013). The ability to rewarm the extremities to beyond the pre-immersion temperature may be possible for several reasons. Firstly, as peripheral temperature is controlled by the sympathetic nervous system (McAllen et al., 2006), feedback responses may cause a time delay, and thus an "overshoot" in temperature may occur. Whilst the vasoconstriction response is rapid, the

skin temperature will present a delayed change (Nagasaka et al., 1987; Romanovsky, 2014). Alternatively, the pattern of rewarming beyond pre-immersion temperature could be attributed to CIVD, where blood vessels to the digits dilate after an initial vasoconstriction response to cold exposure (Lewis, 1930); CIVD is often observed as a delayed significant increase in temperature during prolonged immersion (Daanen, 2003; Cheung, 2015). This CIVD response varies between individuals, both in regards to duration and threshold temperature to elicit a response; the 10-minute interval found in the current study fits several known CIVD patterns (Mekjavic et al., 2008). However, it is unknown whether CIVD still occurs after immersion (Cheung, 2015). Therefore, the increase in average digit temperature beyond baseline during the rewarming period post-immersion requires further investigation.

3.4.4. Conclusion

The current study demonstrated that absolute and relative muscle mass predict heat loss from the hands during severe cold exposure, while weight, height, and fat mass do not. This demonstrates the importance of muscle mass as a thermogenic tissue to maintain extremity temperature; having significant muscle mass when carrying out manual tasks would be advantageous for maintaining thermal balance for populations residing in cold environments. The current study demonstrates the importance of body composition in extremity thermoregulation.

Chapter 4

The thermoregulatory function of the human hand: how do palm and digit proportions affect heat loss?

This paper was published online in the American Journal of Physical Anthropology on 30 March 2018 (Payne et al., 2018b).

Objectives: The current study assessed whether ecogeographical patterns seen in hand proportions correlate with heat loss directly. Using a brief severe cold immersion experiment on the hand, the influence of hand and digit dimensions on heat loss was evaluated.

Materials and Methods: A sample of 113 living individuals were tested. 2-dimensional and 3-dimensional scanning techniques were used to assess hand and digit dimensions. Thermal imaging analysis was used to quantify heat loss during a 3-minute ice-water immersion of the hands.

Results: When body size was accounted for, hand width and digit length relative to total hand length were significant predictors of heat loss from the hand.

Discussion: The current study provides empirical evidence to support the link between thermodynamic principles relating to surface area-to-volume ratio, and ecogeographical patterns associated with temperature.

4.1. Introduction

Human populations are exposed to a wide range of thermal environments and thus have had to evolve a range of physical and behavioural adaptations for thermoregulation

(Parsons, 2014). One trait in particular has historically been the focus of climate adaptation theory: intraspecific variation in surface area-to-volume ratio (Bergmann, 1847; Allen, 1877; Ruff, 1994; Steegmann, 2007). Variation in body size and limb proportions is considered to affect the body's thermoregulatory capacities, and thus, relationships between thermoregulation and variation in the surface area-to-volume ratio of the body have been proposed (Ruff, 1994). However, as the body is not a uniform shape, certain regions may have more thermoregulatory potential than others. The hand, for instance, has a surface area-to-volume ratio five times larger than that of the torso (Molnar, 1957; Hirata et al., 1993; Taylor, 2014), yet the potential role of thermoregulation as a selective pressure contributing to variation in the size and shape of the hand is not well-characterised.

Variation in the surface area-to-volume ratio of the hand could have a significant adaptive advantage in particular climates. Whilst potentially adaptive in hot climates, a hand with a large surface area-to-volume ratio risks significant radiative heat loss in cold conditions, with implications for both cold injury and manual dexterity. As such, hand proportions that contribute to a lower surface area-to-volume ratio may have provided a selective advantage among populations living in cold climates. Indeed, an association seen in digit proportions and climate has been documented among skeletal populations of cold-adapted foragers (Lazenby and Smashnuk, 1999; Betti et al., 2015); populations residing in cold, high latitude regions had relatively shorter and broader first metacarpals than groups from lower latitudes. These results suggest that the predictions of Allen's rule (1877), whereby cold region-inhabiting individuals within a species have shorter, broader appendages than individuals from warmer climes, may apply to human extremities. However, the relationship between hand size and shape and thermoregulation has yet to be tested *in vivo*. The theoretical assumption underlying Allen's rule is that short, broad

appendages reduce surface area-to-volume ratio to minimise heat loss: a form of cold adaptation. Whilst seemingly cold-adapted morphologies may have been shaped by climate, caution must be taken when assuming a direct causal link between the two.

Firstly, the presence of these ecogeographical patterns may be an indirect reflection of factors other than cold adaptation. Patterns that appear to be cold adaptation may be an allometric consequence of differential growth in other body segments (Holliday, 1997b). It has been demonstrated that limb proportions can vary as a result of multiple variables during growth: temperature (Serrat et al., 2008; Serrat, 2013), variable blood flow (Lampl et al., 2003), nutrition (Bogin et al., 2002), or other environmental stresses (Pomeroy et al., 2012). Furthermore, although hand morphology is highly constrained within humans due to functionality (Voracek and Offenmuller, 2007; Xiaohui et al., 2014; Almécija et al., 2015), there is morphological variation that is unrelated to sex or body size differences (Garrett, 1971; Giles and Vallandigham, 1991; Imrhan et al., 1993, 2009; Ashizawa et al., 1997; Imrhan, 2000; Imrhan and Contera, 2005; Mandahawi et al., 2008; Chandra et al., 2011; Dizmen, 2012; Numan et al., 2013). In addition, morphological integration of the hands and feet means that some variation in hand size and shape may be due to covariance between these two regions (Rolian, 2009).

Secondly, Allen's rule treats the appendage as a passive radiating object, which is not the case, as sweat evaporation and vasoregulation will alter the hands' radiative properties (Taylor, 2014). As the hands have a relatively limited capacity for heat production, local tissue temperatures are principally altered by vasoregulation. Vasoconstriction essentially alters the theoretical surface area at which heat is lost from the hand, (Johnson and Proppe, 1996), as the reduction in temperature gradient between the skin's surface and the environment reduces the rate of heat loss, thus potentially minimising any effect that hand size may have on heat loss.

Whether the ecogeographical patterns seen in hand dimensions are directly cold-adaptive remains unknown, as the direct relationship between hand dimensions and heat loss is untested *in vivo* (Steegmann, 2007). Prior research has indicated that hand size is associated with cooling time in cooling experiments on a small sample of volunteers (N=14) (Jay and Havenith, 2004), but this has not been tested on a much larger scale. Thus, the current study aimed to determine whether hand and digit dimensions influence heat loss from the hand in real-time, to test the applicability of cold adaptation theory to the hands.

4.2. Methods

All methods are detailed in Chapter 2. Sampling can be found in section 2.2; anthropometry can be found in section 2.3; experimental protocol can be found in section 2.4.1; thermal image analysis can be found in section 2.5.

4.2.1. Calculations

The following variables were calculated from the anthropometric measures:

$$First\ digit\ ratio = \frac{First\ digit\ width}{First\ digit\ length}$$

$$Third\ digit\ ratio = \frac{Third\ digit\ width}{Third\ digit\ length}$$

$$Digit\text{-}to\text{-}hand\ length\ ratio = \frac{Third\ digit\ length}{Hand\ length}$$

$$Hand\ surface\ area\ to\ volume\ ratio\ (Hand\ SA{:}V) = \frac{Hand\ surface\ area}{Hand\ volume}$$

First digit ratio was calculated as the first digit is known to associate with climate in the skeletal record (Betti et al., 2015). Third digit ratio was calculated as the longest digit and therefore has the potential to have the greatest relationship with heat loss. Digit-to-

hand length ratio was calculated to determine whether the proportions of the finger relative to the hand play a role in heat loss.

To account for any influences of height, the following variables were calculated relative to height: hand length, hand width and hand surface area-to-volume ratio, first digit ratio, third digit ratio, and digit-to-hand length ratio. The corresponding relative variables were calculated as follows:

$$Relative\ variable\ = \frac{Variable}{Height}$$

These relative variables were then used in all statistical analyses.

Average digit temperature immediately after immersion (T_{Post}) was calculated as a percentage of average digit pre-immersion temperature (T_{Pre}), to remove any influence of inter-subject variation in T_{Pre}. Average digit temperature at the proceeding time points (two – T_2, four – T_4, six – T_6, eight – T_8, and ten - T_{10} minutes after immersion) was also calculated as percentages of T_{Pre}.

4.2.2. Statistical Analysis

All continuous variables were assessed for normality using the Shapiro-Wilk Test. Non-parametric tests were applied to variables that were not normally distributed (T_{Post}, T_2, T_4, T_6, T_8, and T_{10}). Anthropometric variables that were not normally distributed, specifically hand surface area and hand volume, were not included in stepwise regression analysis. A paired *t*-test was used to test for differences in pre-immersion core temperature and core temperature during the final minute of immersion. Stepwise regression analysis was carried out to determine whether hand length, hand width or hand surface area-to-volume ratio relative to height could predict T_{Post} in the following model:

Model

$T_{Post} = \beta_0 + \beta_1$[relative hand length] + β_2 [relative hand width] + β_3 [relative hand SA:V]

Spearman's Rank correlation analysis was used to determine whether any hand variables correlated with T_{Post}, T_2, T_4, T_6, T_8, T_{10}. The percentage change in average digit temperature between each adjacent time point was calculated: Change between T_{Post} and T_2, T_2 and T_4, T_4 and T_6, T_6 and T_8, and T_8 and T_{10}. To reach a normal distribution, a square-root transformation was applied to each percentage change calculation (T_{Post}-T_2, T_2-T_4, T_4-T_6, T_6-T_8, and T_8-T_{10}). Linear regression analysis was then carried out to determine if any hand variables were significant predictors of percentage change in average digit temperature at each time interval.

All statistical analysis was carried out using SPSS 25.0 for Windows.

4.3. Results

4.3.1. Test Sample Statistics

Table 4.1 summarises the anthropometric variables of the test sample. Height, hand length, hand width, and hand SA:V were approximately normally distributed. Hand surface area and hand volume were normally distributed when grouped by sex. As there were no significant differences between the sexes in anthropometric variables relative to height, the sexes were pooled for the analyses.

Table 4.1 Summary statistics of anthropometric variables

	N	Minimum	Maximum	Mean (SD)
Height (cm)	113	150.1	200.0	175.0 (±9.2)
Relative Hand Length	113	0.0984	0.1168	0.1073 (±0.00358)
Relative Hand Width	113	0.0399	0.0546	0.0455(±0.00269)
Relative Hand SA:V	105	0.00005	0.00009	0.00007(±0.00001)
Relative First Digit Ratio	113	0.00014	0.00024	0.00019(±0.00002)
Relative Third Digit Ratio	113	0.00009	0.00018	0.00013(±0.00001)
Relative Digit-to-Hand Ratio	113	0.00022	0.00030	0.00025(±0.00002)

SD: standard deviation; first digit ratio – first digit width/first digit length; third digit ratio – third digit width/third digit length; digit-to-hand length ratio – third digit length/hand length

4.3.2. Heat loss

There was no significant difference in core body temperature before immersion (36.85˚C, ±0.38) and in the final minute of immersion (36.83˚C, ±0.35) (t_{112}=-0.840, p>0.05)

Relative hand length was not a significant predictor of heat loss in any model. Relative hand width was a significant predictor alone (Figure 4.1A), but the model of best fit included both relative hand width and relative digit-to-hand length ratio (Table 4.2 & Figure 4.1B).

Table 4.2 Summary of stepwise linear regression predicting TPost.

Model	Predictor	B	Std. Error	β	p-value	R^2
1	**(Constant)**	8.948	7.931		>0.05	
	Relative hand width	745.299	173.985	0.389	<0.01	0.151**
2	**Constant**	26.761	10.585		<0.05	
	Relative hand width	721.794	170.107	0.377	<0.01	
	Relative digit-to-hand length ratio	-66769.394	27058.198	-0.219	<0.05	0.199**

***= highly significant (p<0.01). In model 1, excluded variables = relative hand length, relative hand SA:V, relative digit-to-hand length ratio; In model 2, excluded variables = relative hand length, relative hand SA:V*

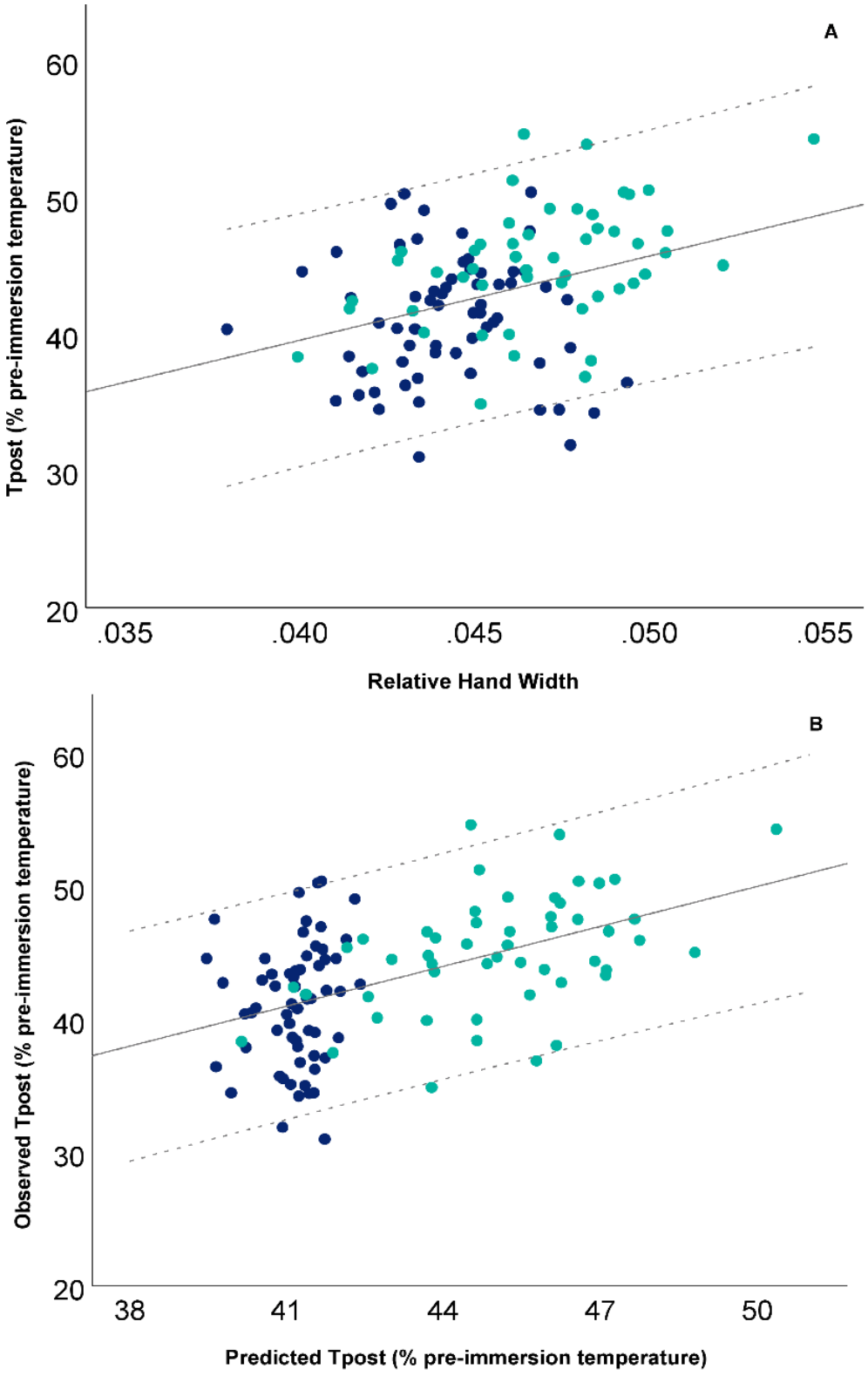


*Figure 4.1 Scatterplots of model 1 and model 2 from regression analyses. Blue: female, Green: male. Panel A: Scatterplot of relative hand width and TPost Regression line: y=13.99+636*x, R2=0.151 Panel B: Scatterplot of predicted TPost,, using model 2 from regression analyses, and observed TPost . Regression line: y=-9.24E-14+1*x, R2=0.199*

4.3.3. Hand and digit dimensions and average digit temperature by time point

The results of Spearman's rank correlation analysis assessing the relationship between relative hand length, hand width and hand surface area-to-volume ratio and temperature at each time point after immersion are summarised in Table 4.3. Relative hand width significantly positively correlated with T_{Post}, while relative hand length did not. Relative digit-to-hand length ratio also correlated with T_{Post}, while neither relative first digit ratio, nor third digit ratio correlated with temperature at any of the time points. Relative hand SA:V significantly negatively correlated with T_{Post} and T_2. No hand size variable correlated with average digit temperature beyond T_2.

Table 4.3 Summary of Spearman's rank correlation analysis between hand size variables and average digit temperature during the experiment

Average digit temperature (% of pre-immersion temperature) at given time point after immersion		**0 mins (T_{Post})**	**2 mins (T_2)**	**4 mins (T_4)**	**6 mins (T_6)**	**8 mins (T_8)**	**10 mins (T_{10})**
Relative Hand Length	**CC**	0.157	-0.036	-0.102	-0.061	-0.103	-0.152
	Sig. (2-tailed)	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Relative Hand Width	**CC**	0.333**	0.184	0.141	0.148	0.113	0.082
	Sig. (2-tailed)	<0.01	>0.05	>0.05	>0.05	>0.05	>0.05
Relative Hand SA:V Ratio	**CC**	-0.320**	-0.302**	-0.068	-0.042	-0.047	-0.010
	Sig. (2-tailed)	<0.01	<0.01	>0.05	>0.05	>0.05	>0.05
Relative first digit ratio	**CC**	0.060	-0.015	-0.058	-0.002	-0.021	0.011
	Sig. (2-tailed)	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Relative third digit ratio	**CC**	-0.061	-0.080	-0.048	-0.056	-0.073	-0.078
	Sig. (2-tailed)	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Relative digit-to-hand length ratio	**CC**	-0.262**	-0.184	-0.037	0.017	-0.020	0.028
	Sig. (2-tailed)	<0.01	>0.05	>0.05	>0.05	>0.05	>0.05

*CC= Correlation Coefficient; *=p<0.05; **=p<0.01*

4.3.4. Hand dimensions as predictors of temperature change and reheating

The only significant predictor of temperature change in any interval was relative hand length between T_{Post} and T_2 (Table 4.4 & Figure 4.2A) and relative third digit ratio between T_6 and T_8 (Table 4.4 & Figure 4.2B). No other variable predicted change in temperature at any time interval.

Table 4.4 Summary of regression models of hand dimensions as predictors of change between TPost and T2

Model	Predictors	B	Std.Error	β	P value	R^2
T_{Post}-T_2	**(Constant)**	8.725	2.713		<0.01	
	Relative Hand Length	-50.946	25.308	-0.195	<0.05	0.038*
T_6-T_8	**(Constant)**	1.080	0.733		>0.05	
	Relative 3rd digit ratio	11461.654	5716.212	0.191	<0.05	0.037*

*TPost-T2 Model, excluded variables: relative hand width, relative hand SA:V, relative 1st digit ratio, relative digit-to-hand length ratio; T6-T8 Model, excluded variables: relative hand length, relative hand width, relative hand SA:V, relative 1st digit ratio, relative digit-to-hand length ratio. Std. Error = Standard Error, *= p<0.01*

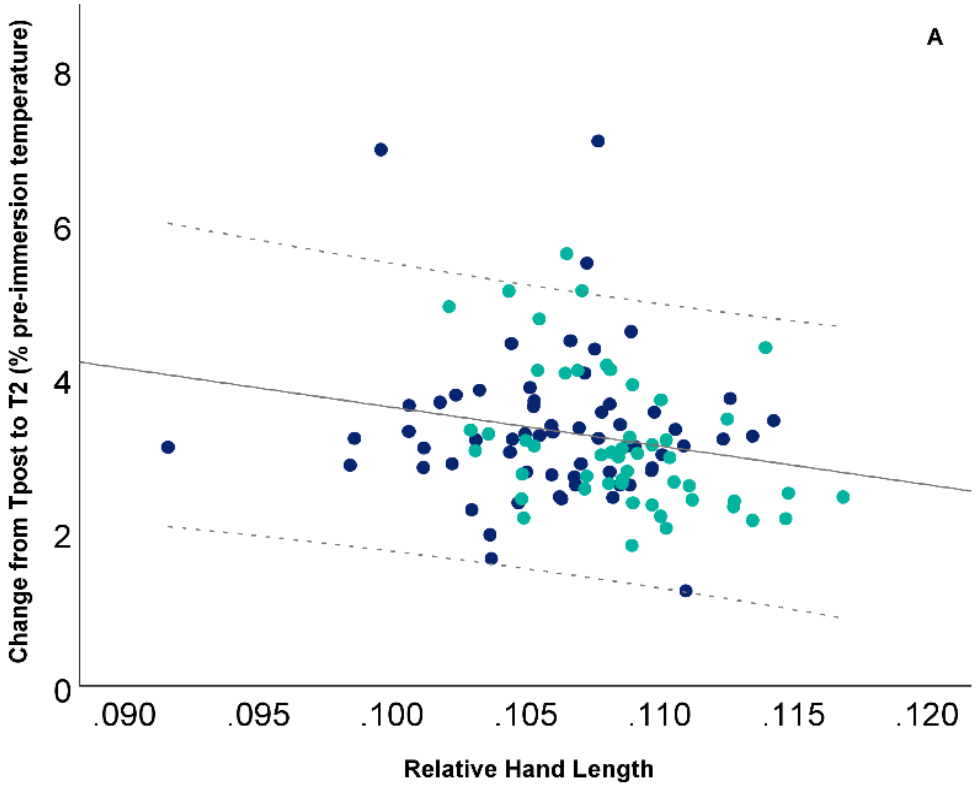


Figure 4.2

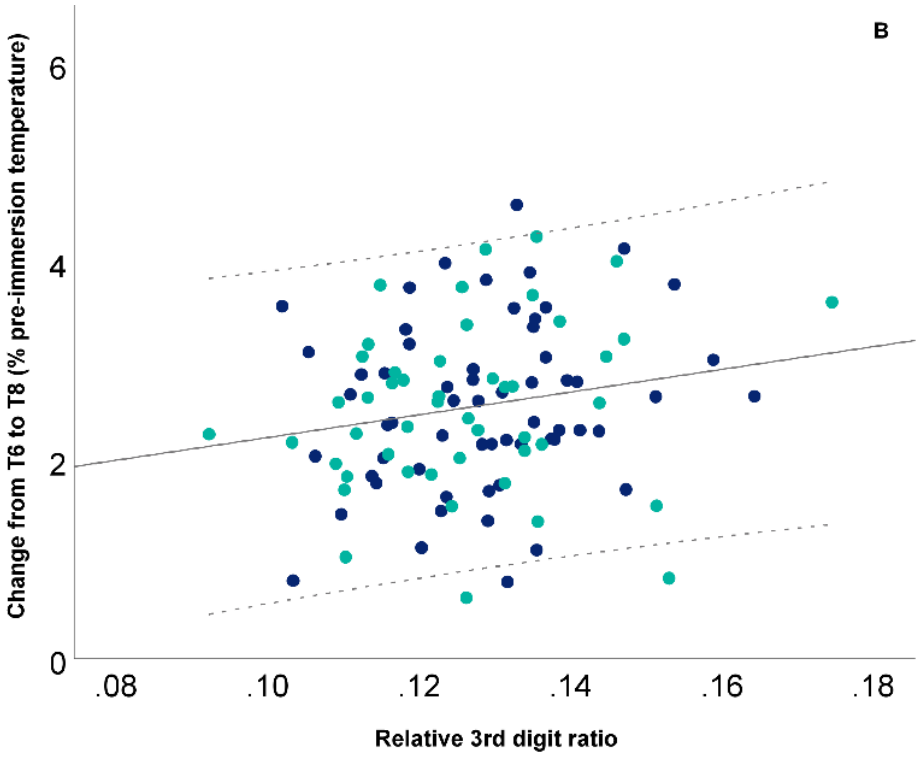


Figure 4.2 Scatterplots of hand dimensions as a predictor of temperature change at given time intervals. Blue: female, Green: male.

*Panel A: Relative hand length against change in average digit temperature between TPost and T2. Regression line: y=9.75-60.49*x. R^2=0.038 Panel B: Relative third digit ratio against change in average digit temperature between T6 and T8. Regression line: y=8.64-50.23*x. R^2=0.037*

4.4. Discussion

The current study indicated that hand dimensions could play a role in heat loss from the hand. Whilst this had been demonstrated in cooling experiments on a small sample (Jay and Havenith, 2004), the findings here demonstrate this relationship on a larger scale. Wider hands with shorter digits relative to overall hand length have a smaller surface area-to-volume ratio and lose less heat upon ice-water immersion than narrower hands with longer digits. Thus, wide hands and relatively short digits could be more advantageous in cold environments as heat loss would be reduced and risk of cold injury minimised. The current study supports the underlying thermodynamic principles behind Allen's rule, documenting a relationship between thermoregulation and variation in hand morphology *in vivo*. These results suggest that thermoregulation in the hand may thus have been one of

the selection pressures contributing to human variation in hand and digit proportions in our evolutionary history.

These results highlight relative hand width and digit-to-hand length ratios as significant predictors of heat loss from the hand. This finding aligns with the thermodynamic principles relating to heat radiation (Taylor, 2014), whereby appendage dimensions that create a greater surface area-to-volume ratio will result in greater heat loss. Notably, relative hand width is the most influential predictor of heat loss, as a small increase in width will result in a significant increase in volume but a small increase in surface area, compared to an increase in hand length, reinforcing the cylindrical model of the human body or appendages for radiating heat (Ruff, 1994). Ruff demonstrated that body width significantly correlates with latitude, further supporting the idea that variation in body width may have developed in response to environmental temperature stresses, although other confounding factors may have also influenced this pattern. Though such whole-body models of heat loss may not always be applicable to limbs in isolation (Collard and Cross, 2017), results of the current study suggest that the same relationships between width and thermoregulation may apply within the upper limb segment, specifically to the hand. Further, by documenting a relationship between wider hands with relatively short fingers and less heat loss per unit volume, our *in vivo* findings support the underlying theoretical basis of Allen's rule, by which individuals inhabiting cold environments would be predicted to have shorter appendages than individuals inhabiting tropical environments (Niles, 1973; Lindsay, 1987; Rasmussen, 1994; Fooden and Albrecht, 1999; Nudd and Oswald, 2007). The results from the current study also align well with the ecogeographic variation in first and second metacarpal dimensions (Lazenby and Smashnuk, 1999; Betti et al., 2015). Although the first and second metacarpals themselves were not measured here, these bones are tightly integrated into hand development, and thus are likely to relate

to other hand elements. Further research is required to determine whether length and width of metacarpals associate with digit temperatures.

Not only was there substantial variation in heat loss attributable to morphological variation in the hands, but there was also substantial variation in rewarming patterns following cold exposure that bore apparent relationships with morphology. For example, relative hand length was a significant predictor of initial rewarming temperature, whereby relatively longer hands did not rewarm as quickly as relatively shorter hands. Such a relationship may reflect the longer distance for blood to travel before reaching digit extremities during reheating, and supports the distal blood flow hypothesis (Lampl et al., 2003), whereby limited nutrients cause a reduction in energetic investment in distal limb elements. In the current study, limited heat means that it takes longer for heat to be transferred to distal elements once cold. The distal blood flow hypothesis may also explain variation in temperature change that occurred much later in the rewarming period, between minutes six and eight. At this time, the relative third digit ratio was found to predict change in temperature, with wider third digits relative to length being associated with a greater increase in temperature. This suggests that individuals with particularly long fingers may be more prone to cold injury, as their digits will take longer to return to a temperature which avoids tissue freezing. Alternatively, this observed delayed influence of digit proportions on rewarming may result from a delayed vasodilatation response (Wendt et al., 2007), whereby vasomotor responses adapt within a particular individual to minimise heat loss in areas that have a particularly high surface area-to-volume ratio for that individual (Yoshimura et al., 1952). Vasoregulation was not directly measured in the current study, but it can significantly influence hand and digit temperatures (Daanen, 1997; Cheung and Daanen, 2012; Cheung, 2015), so may partly explain the significant variation in average digit temperature documented in Figure 4.1 and Figure 4.2.

Cold immersion in the current study involved immersion in ice-water, so the cooling rates observed here are likely to be faster than would occur among individuals exposed to cold air temperatures in field conditions. This is because cold injury rate is dependent upon the medium (air or water) to which heat is lost (Nimmo, 2004); heat is lost to water approximately 3-5 faster than air at the same temperature (Molnar, 1946). However, many indigenous populations inhabiting cold environments rely heavily on marine or aquatic resources, and resource acquisition likely involves frequently undertaking manual tasks while exposed to cold water (Makinen, 2010). Populations living in Arctic marine environments are indeed found to have hand elements, specifically the second metacarpal, optimised to reduce heat loss (Lazenby and Smashnuk, 1999). Further investigation is required to determine whether other groups inhabiting similar environments have similar hand and digit proportions, such as Tasmanian aboriginal groups (Gilligan, 2014), and Tierra del Fuegan indigenous groups (De La Fuente et al., 2015).

4.4.1. Conclusion

The current study indicates that hand dimensions directly affect heat loss during cold exposure, providing experimental support for thermoregulation as a selective pressure contributing to variation in human hand proportions. The findings here align with climate adaptation patterns found in the skeletal record (Lazenby and Smashnuk, 1999; Betti et al., 2015) whereby cold environments are associated with shorter, broader digit elements. Specifically, these results show that wide hands with relatively short digits are seen to lose less heat *in vivo* than narrow hands with relatively long digits, and thus align with the underlying principles behind Allen's rule.

Chapter 5

The influence of digit size and proportions on dexterity during cold exposure

This paper was published online in the American Journal of Physical Anthropology on 20 April 2018 (Payne et al., 2018c). An expanded literature review has been added for the purpose of completeness in this thesis.

Objectives: The current study investigated whether size and proportions of the hands and digits affect dexterity during severe cold exposure. As wide hands are known to lose less heat than narrow hands, and narrow digits are associated with greater dexterity, this study aimed to test whether there was a direct trade-off between dexterity and thermoregulation that shapes hand morphology.

Methods: Participants (25 women, 15 men) carried out the Purdue pegboard test before and after a 3-minute ice-water immersion of the hand. Their hand length, hand width, digit lengths, and digit widths were measured using standard anthropometric methods.

Results: Wide first and third digits associated with significantly reduced dexterity after immersion relative to individuals with narrower first and third digits. Second digit width positively correlated with average digit temperature after immersion. Hand length and hand width did not influence dexterity.

Conclusion: The current study suggests that digit width influences dexterity in cold conditions, reflecting patterns found at room temperature. Hand and digit morphology may

be the product of two significant constraints on the hand: dexterity and thermoregulation. In cold conditions, hand morphology appears to be predominantly constrained by thermal stress, at the expense of dexterity. This may have important implications for interpreting the morphology of extinct and extant hominins.

5.1. Introduction

The intraspecific variation in hand and digit proportions is significantly smaller in humans than in other hominoid species, indicating strong selection for our specific proportions (Almécija et al., 2015; Kivell, 2015). Whilst human hand proportions may be highly constrained by morphological integration of the hands and feet (Rolian, 2009), variation may also be further constrained by selection for manual dexterity: the ability to carry out skilful well-coordinated hand and finger manipulations (Fleishman and Ellison, 1962). Indeed, even under severe energetic stress, such as that experienced by highland Peruvian populations, hand proportions relative to body size are seen to be preserved at the expense of other limb segments, demonstrating the prioritisation of hand proportions to maintain their manipulatory function (Pomeroy et al., 2012). The preservation of these proportions reflects the functional importance of the hand for fine motor activities. However, hand and digit proportions may be constrained not only by morphological integration and selection for manipulation but may also be shaped by climate.

As the hand has the highest surface area-to-volume ratio of any body part (Molnar, 1957; Hirata et al., 1993; Taylor, 2014), the hand's capacity for heat loss may also be of adaptive value. Quantifying digit proportions in skeletal remains has indicated that there are ecogeographic patterns in digit morphology (Lazenby and Smashnuk, 1999; Betti et al., 2015). These findings indicated that hand proportions might be climate-adapted; hand proportions were considered to align with Allen's Rule (Allen, 1877), whereby appendage length and width associated with climate to reduce surface area-to-volume ratio for heat

conservation. Experimental research *in vivo* on heat loss from the hands demonstrates that wide hands with relatively short digits do retain more heat in cold conditions (Payne et al., 2018b). However, the effect of hand and digit proportions on maintaining digit temperatures is likely to be relatively moderate in comparison to the effect of physiological adaptations such as vasoregulation (Sloan and Keatinge, 1973; LeBlanc, 1975; Smith and Hanna, 1975; Hayward and Keatinge, 1981; Chudecka, 2013; Taylor, 2014; Tanda, 2016). In particular, CIVD is seen to maintain peripheral temperatures in populations exposed to severe cold (Lewis, 1930; Cheung, 2015), such as highland Peruvians (Little, 1976) and indigenous Arctic populations (Brown et al., 1953; Page and Brown, 1953; Meehan, 1955; Elsner et al., 1960; LeBlanc, 1975; Steegmann, 1977), and is thought to become enhanced during growth (Frisancho, 1993). In addition, CIVD is known to maintain dexterity during cold exposure (Cheung, 2015; Cheung et al., 2016). However, there is currently no consensus as to whether selection for such a trait occurred to reduce fatal cold injury or maintain dexterity (Hanna and Brown, 1983; Daanen, 2003; Wilberfoss, 2012; Cheung, 2015). Whether morphological adaptations to maintain digit temperature have developed alongside these physiological mechanisms is unknown. Whilst vasoregulation is likely to primarily influence digit temperatures, associations between hand morphology and digit temperatures are still seen (Payne et al., 2018b), suggesting that selection may also act upon morphology to further aid the maintenance of peripheral temperatures. Whether hand morphology has any influence on their manipulatory function remains to be seen.

Digit proportions are known to influence dexterity at room temperature, whereby individuals with wider digits (Marshall, 2007), and wider palms with relatively short thumbs (Çakit et al., 2016), tend to have decreased performance on standardised dexterity tests. This association is seen to be stronger in the non-dominant hand (Şahin et al., 2017). However, this association between wide digits and lower dexterity scores is somewhat

dependent on the nature of the task (Peters and Campagnaro, 1996). In standardised pegboard tests, when wide pegs are included, those with wider digits tend to perform better than those with slim digits, who instead perform better with finer pegs. When assessing grip strength, individuals with wider and longer hands tended to have higher grip strength than those with small hands, and individuals with a wide span between first and fifth digit tip with the fingers outstretched also tended to have a higher grip strength than those with a narrow finger span (MacDermid et al., 2002). Whilst the influence of digit proportions on dexterity has been established in room temperature conditions, this relationship has yet to be tested in cold conditions. It is well established that dexterity is significantly compromised in cold conditions (Horvath and Freedman, 1947; Teichner, 1957; Gaydos and Dusek, 1958; Clark, 1961; Schiefer et al., 1984), but how this relationship is affected by hand and digit morphology is not known.

If the association between digit width and dexterity observed at room temperature is also seen in cold conditions, then a trade-off may arise between dexterity and thermoregulation. Wide hand and digit proportions, advantageous for heat retention, would be costly for dexterity. If wide hands and digits lose dexterity on cold exposure, then thermal stress may be the primary selective pressure in cold conditions, as wider proportions are found in cold-inhabiting populations, such as Inuit, Inupiat, and Fuegian groups (Lazenby and Smashnuk, 1999; Betti et al., 2015). Cold may be the dominant selective pressure as severe cold injury and hypothermia are likely to be more detrimental in the long term than loss of fine finger dexterity. The opposing hypothesis, whereby dexterity is not influenced by hand and digit proportions or improves with hand or digit width during cold exposure, would suggest that both thermal stress and dexterity may be dual selective pressures promoting the same hand and digit morphology. Arguably, morphology that promotes the maintenance of fine motor control when performing manual

tasks essential for survival in cold conditions could be a significant advantage (Taylor, 2014). As cold region-inhabiting populations are found to have shorter, broader proportions of their metacarpals (Lazenby and Smashnuk, 1999; Betti et al., 2015), these may be the optimal proportions for maintaining dexterity in these conditions for tasks such as hunting, food preparation, fire-lighting, and shelter maintenance (Cheung, 2015). Thus, determining whether hand proportions affect dexterity in cold conditions may shed further light on whether ecogeographic patterns in hand proportions have adaptive value.

Studying the influence of hand proportions on dexterity in the cold is particularly challenging, as there are multiple physiological contributors to the cold-associated decrease in manual dexterity. As discussed in previous chapters, vasoregulation can significantly alter blood flow, and during cold exposure constriction of blood vessels in the digits can result in a flow rate close to zero at the fingertips (Rowell, 1974; Johnson and Proppe, 1996). As a consequence, hand temperatures can reach below 10˚C in several minutes (Mills, 1956; Geng, 2001). This has an impact on the functioning of multiple soft tissues in the hand; nerves, muscles, joints and ligaments are all affected by temperature changes. Cold can reduce nerve conduction velocity (De Jong et al., 1966; Vanggaard, 1975), and at nerve temperatures below 10˚C, nerve conduction entirely ceases. Fortunately, neuronal axons are located within deeper structures, and thus nerve temperature will follow skin temperature after significant delay, allowing nerve conduction velocity to be maintained for as long as possible on cold exposure (Heus et al., 1995). Exposure of muscle to temperatures below 28˚C reduces maximal contraction velocity and force, and reduces time to exhaustion, affecting contraction force of the fingers and hand (Clarke et al., 1958). Finger mobility is determined by joint mobility, which in turn is influenced by the viscosity of synovial fluid. Synovial fluid viscosity increases in cold conditions causing significant joint stiffness. Along with reduced mobility, changes to motor control due to decreased

tactile sensitivity can also occur (Provins and Morton, 1960), and can cause underestimation of handgrip force and plantar pressure, possibly resulting from proprioceptive suppression (Nurse and Nigg, 2001; Cheng et al., 2014). Motor control progressively decreases proportionally to the volume of limb exposed to cold (Montgomery et al., 2015). Overall, a reduction in temperature and blood flow has significant negative effects on manual dexterity. Variation in hand proportions may have no effect on dexterity in the cold as a result of the multiple tissues compromised by low temperatures, but this remains to be tested.

Understanding the relationships between morphology, dexterity, and thermoregulation are also important for interpreting the morphology of skeletal remains from modern humans and extinct hominins, and in turn inferring behaviours in a climatic context. For example, whilst the dextrous capacities of *Homo neanderthalensis* (Neanderthals) are likely to have been near identical to anatomically modern humans, based on evidence from mathematical and three-dimensional modelling (Niewoehner et al., 2003; Feix et al., 2015), material culture (Niewoehner, 2006), and representational art (Hoffmann et al., 2018), the possible compromise on dexterity experienced by high latitude-dwelling Neanderthal groups remains unknown. When considering morphological evidence, the comparative length of metacarpals between Neanderthals and modern humans indicates that Neanderthals had longer palms relative to their digits (Musgrave, 1971; Mersey et al., 2013). This would indicate that their hands may have remained warmer in cold conditions, based on the experimental results of Payne *et al.* (2018b). However, it is not possible to make inferences about how vasoregulation may have affected Neanderthal extremity temperature. Whilst Neanderthal populations spanned a broad range of climates (Krause et al., 2007; Hublin and Roebroeks, 2009), this finding is of particular interest relating to Neanderthal fossil remains found in high latitude regions

(Nielsen et al., 2017), as their hand proportions may have been better suited to maintaining thermal balance in cold climates. However, the extent to which their hand proportions affected Neanderthal dexterity in cold conditions cannot be inferred without reference data from living populations.

The current study provides an empirical test of the relationship between manual dexterity and variation in the proportions and temperature of the hand and digits after acute cold exposure among living men and women. In doing so, the study aimed to assess the functional significance of specific hand proportions in cold environments and whether this reflects a trade-off between thermoregulation and dexterity. This indicates how selection for dexterity or thermoregulation may be contributing to both ecogeographic variation in human hand proportions and hand morphology of extinct hominins.

5.2. Methods

All methods are detailed in Chapter 2. Sampling can be found in section 2.2.2; anthropometry can be found in section 2.3.2; experimental protocol can be found in section 2.4.2; thermal image analysis can be found in section 2.5.

5.2.1. Calculations

The first, second, and third digits were included in the calculations.

Digit-to-hand length ratio was then calculated as follows:

$$Digit\text{-}to\text{-}hand\ length\ ratio = \frac{Third\ digit\ length}{Hand\ length}$$

Individual digit ratios were calculated as follows:

$$Digit\ ratio = \frac{Digit\ width}{Digit\ length}$$

The dexterity test before immersion ($DEX_{Pre)}$ and immediately after immersion (DEX_{Post}) were used to calculate any difference in dexterity (DEX_{Diff}):

$$DEX_{Diff} = DEX_{Pre} - DEX_{Post}$$

5.2.2. Statistics

The Shapiro-Wilk test was used to determine whether variables were normally distributed. Where variables were found to be normally distributed, independent sample *t*-tests were carried out to determine differences between males and females in anthropometric variables. In the case where there were no significant differences in hand or digit proportions between the sexes, sexes were pooled. In the instances where variables were non-normally distributed, Spearman's rank correlation coefficient analysis was used to determine any relationships between anthropometric variables, dexterity, and temperature using a p-value of 0.05 to assess significance. Independent sample *t*-tests were used to assess any differences in dexterity between the sexes. A paired *t*-test was used to test for differences in pre-immersion core temperature and core temperature during the final minute of immersion. All statistical analysis was carried out using SPSS 25.0 for Windows.

5.3. Results

Table 5.1 summarises the anthropometric variables of the test sample. Independent sample *t*-tests demonstrated that there were no differences between males and females in hand and digit measurements, other than hand length (t_{38}=4.201, p<0.01), hand width (t_{38}=5.389, p<0.01), second digit length (t_{38}=2.433, p<0.05), and second digit width (t_{38}=2.542, p<0.05). When sexes were pooled, hand width, first digit length, first digit width, and second digit width were normally distributed, as was height. Hand length,

second digit length, third digit length, third digit width, weight, and digit-to-hand length ratio were not normally distributed. Thus, non-parametric tests were applied.

There was no significant difference in core body temperature before immersion (36.81˚C, ±0.35) and in the final minute of immersion (36.81˚C, ±0.35) (t_{39}=-0.201,p>0.05).

There was no correlation between pre-immersion dexterity (DEX_{Pre}) and any hand or digit dimensions. Post-immersion dexterity (DEX_{Post}) and the difference in dexterity before and after immersion (DEX_{Diff}) did not correlate with the following anthropometric variables: hand length, hand width, digit-to-hand length ratio, first digit ratio, and third digit ratio.

Table 5.1 Summary statistics of combined sample (males and females)

	Minimum	**Maximum**	**Mean (SD)**
Hand Length (cm)	16.10	20.00	17.94 (±1.12)
Hand Width (cm)	6.20	8.40	7.19 (±0.60)
First digit length (cm)	4.50	6.60	5.57 (±0.49)
First digit width (cm)	1.40	2.20	1.76 (±0.19)
First digit ratio	0.25	0.40	0.32 (±0.04)
Second digit length (cm)	6.10	7.70	6.87 (±0.48)
Second digit width (cm)	1.30	2.20	1.72 (±0.20)
Second digit ratio	0.19	0.33	0.25 (±0.03)
Third digit length (cm)	7.00	9.10	7.75 (±0.58)
Third digit width (cm)	1.40	2.00	1.70 (±0.17)
Third digit ratio	0.17	0.27	0.22 (±0.02)
Digit-to-hand length ratio	0.40	0.50	0.43 (±0.02)
Height (cm)	152.2	191.5	166.9 (±9.3)
Weight (kg)	42.40	100.95	62.64 (±15.15)

SD: Standard Deviation

First digit width was found to significantly correlate with $DEX_{Diff,}$ and negatively correlate with DEX_{Post} (**Error! Not a valid bookmark self-reference.** and Figure 5.1A). Third digit width was also found to negatively correlate with DEX_{Post} (Table 5.4 and Figure 5.1B). No other correlations were found between the dexterity variables and digit widths or lengths.

Table 5.2 Summary of Spearman's Rank Analysis of first digit variables, dexterity and average digit temperature

	First digit length		**First digit width**		**First digit ratio**	
	CC	**Sig.**	**CC**	**Sig.**	**CC**	**Sig.**
DEX_{Diff}	0.236	ns	0.448**	p<0.01	0.264	ns
DEX_{Pre}	0.071	ns	-0.024	ns	-0.061	ns
DEX_{Post}	-0.150	ns	-0.433**	p<0.01	-0.210	ns
Pre-immersion temperature	-0.043	ns	-0.126	ns	-0.074	ns
Post-immersion temperature	-0.208	ns	-0.021	ns	0.175	ns

*CC= Correlation coefficient; Sig.= Significance; ns=not significant *= significant (p<0.05); **= highly significant (p<0.01)*

Table 5.3 Summary of Spearman's Rank Analysis of second digit variables, dexterity and average digit temperature

	Second digit length		**Second digit width**		**Second digit ratio**	
	CC	**Sig.**	**CC**	**Sig.**	**CC**	**Sig.**
DEX_{Diff}	0.084	ns	-0.271	ns	-0.298	ns
DEX_{Pre}	0.01	ns	-0.068	ns	-0.054	ns
DEX_{Post}	-0.062	ns	0.160	ns	0.208	ns
Pre-immersion temperature	-0.112	ns	0.260	ns	0.283	ns
Post-immersion temperature	0.018	ns	0.369*	p<0.05	0.29	ns

*CC= Correlation coefficient; Sig.= Significance; ns=not significant *= significant (p<0.05); **= highly significant (p<0.01)*

Table 5.4 Summary of Spearman's Rank Analysis of third digit variables, dexterity and average digit temperature

	Third digit length		Third digit width		Third digit ratio	
	CC	**Sig.**	**CC**	**Sig.**	**CC**	**Sig.**
DEX_{Diff}	0.127	ns	0.263	ns	0.153	ns
DEX_{Pre}	-0.126	ns	-0.086	ns	-0.024	ns
DEX_{Post}	-0.2	ns	-0.353*	p<0.05	-0.138	ns
Pre-immersion temperature	-0.005	ns	0.008	ns	0.109	ns
Post-immersion temperature	-0.226	ns	0.097	ns	0.356*	p<0.05

*CC= Correlation coefficient; Sig.= Significance; ns=not significant *= significant (p<0.05); **= highly significant (p<0.01)*

Second digit width and third digit ratio correlated with post-immersion average digit temperature (

Table 5.3 and Figure 5.2). No other digit lengths or widths correlated with average digit temperature at any time point. DEX_{Pre}, DEX_{Post}, or DEX_{Diff} did not correlate with average digit temperature at any time point.

There were no differences in dexterity between the sexes. There was no significant difference in core body temperature before immersion and in the final minute of immersion.

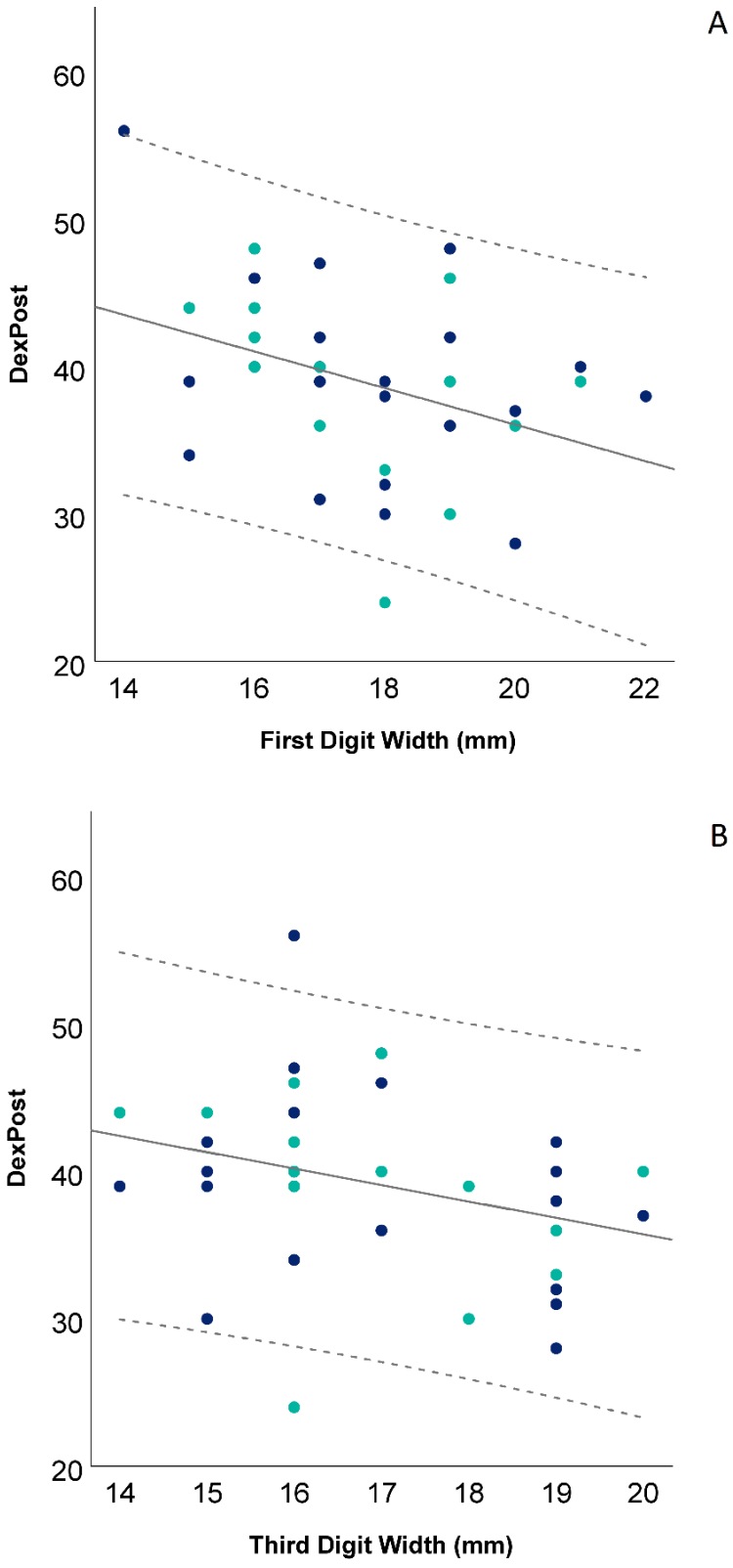


Figure 5.1 Scatterplots of dexterity and digit widths. Blue: female, Green: male. A. Scatterplot of first digit width and DEXPost. Correlation Coefficient=-0.433; B. Scatterplot of third digit width and DEXPost. Correlation Coefficient=-0.353.

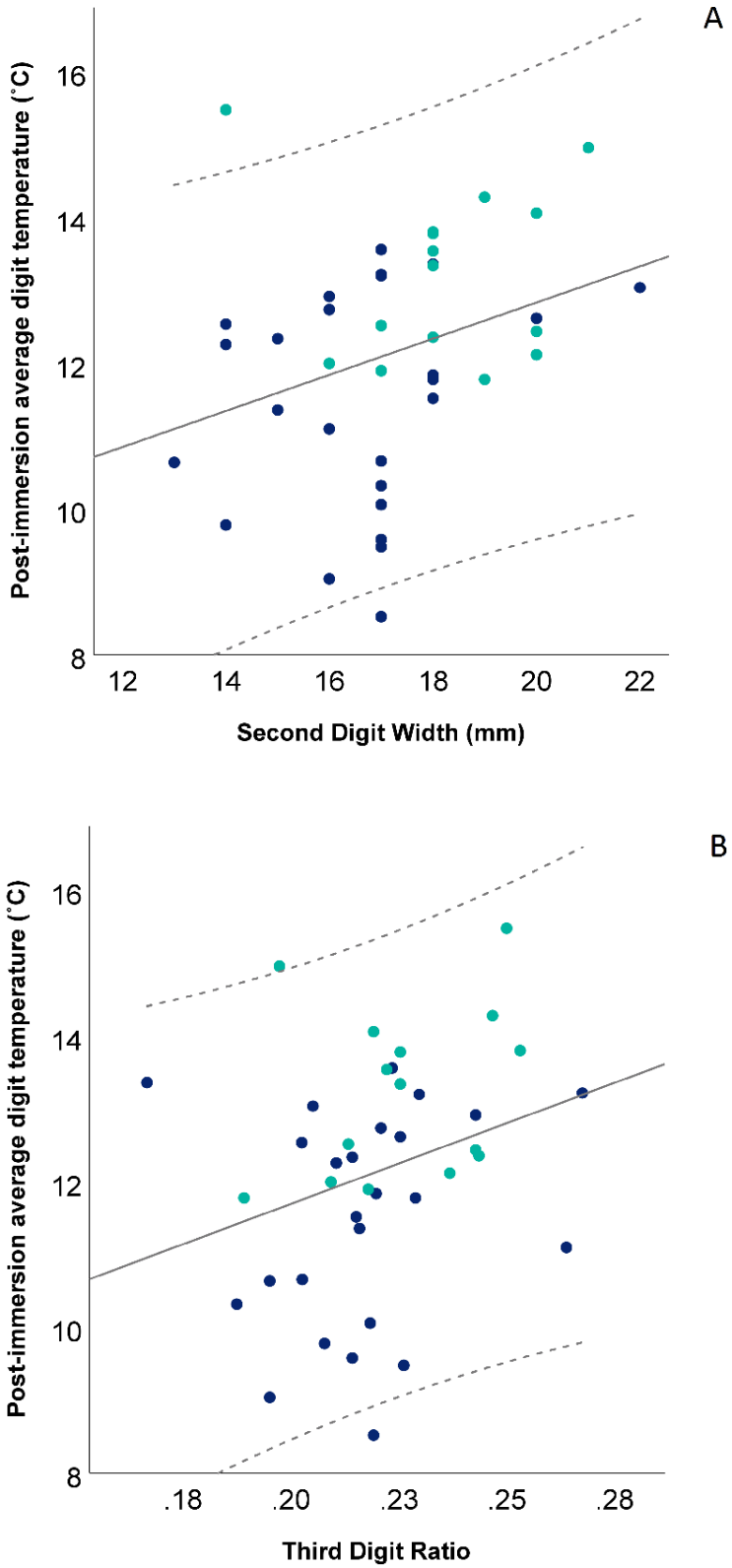


Figure 5.2 Scatterplots of post-immersion average digit temperature and anthropometric variables. Blue: female, Green: male. A. Scatterplot of second digit width and post-immersion average digit temperature. Correlation Coefficient=0.369; B. Scatterplot of third digit ratio and post-immersion average digit temperature. Correlation Coefficient=0.356.

5.4. Discussion

The current study suggests that digit dimensions affect dexterity under cold conditions: individuals with wider first and third digits had significantly reduced dexterity after immersion relative to individuals with narrower digits. Individuals with a wider first digit also had a greater difference in dexterity between the pre-immersion dexterity test and the post-immersion dexterity test than those with a narrower first digit. These results reflect the association observed between digit width and dexterity at room temperature (Marshall, 2007; Şahin et al., 2017). Second digit width did not influence dexterity in cold conditions but associated with average digit temperature after immersion, as did third digit ratio. Dexterity did not correlate with digit length, hand length, hand width or digit-to-hand length ratio. These results suggest that narrow digits are more advantageous for carrying out dextrous tasks in cold conditions than wide digits, but compromise digit temperature.

The current study suggests that there is a trade-off between manual functions in cold conditions: dexterity and thermoregulation. Wider hands with relatively short and wide digits maintain a higher average digit temperature (Payne et al., 2018b). However, wide digits are seen to reduce dexterity, although length and width of hands do not appear to affect dexterity in this case. This indicates that only certain hand dimensions impact on dexterity and thermoregulation (Figure 5.3).

The current study suggests that first digit width significantly influences fine finger dexterity during cold exposure. This aligns with previous research, which demonstrates that the first digit is essential in performing the precision pinch grips required for fine finger dextrous tasks (Napier, 1960; Fleishman and Ellison, 1962; Boesch and Boesch, 1993; Bernstein, 1996; Yancosek and Howell, 2009). Second digit width did not influence dexterity in cold conditions but associated with average digit temperature. The second digit is the first to receive blood from the superficial palmar arch (Standring, 2008), as the first

digit has a separate blood supply linked to the radial artery. Vasoconstriction may affect the second digit strongly and thus significantly reduce temperature, and thus reflect the temperature across the other digits. Third digit width negatively correlated with dexterity. Although not a commonly used digit in the Purdue pegboard dexterity test, this dimension may correlate with dexterity as a result of significant integration with other elements of the hand, such as the first digit.

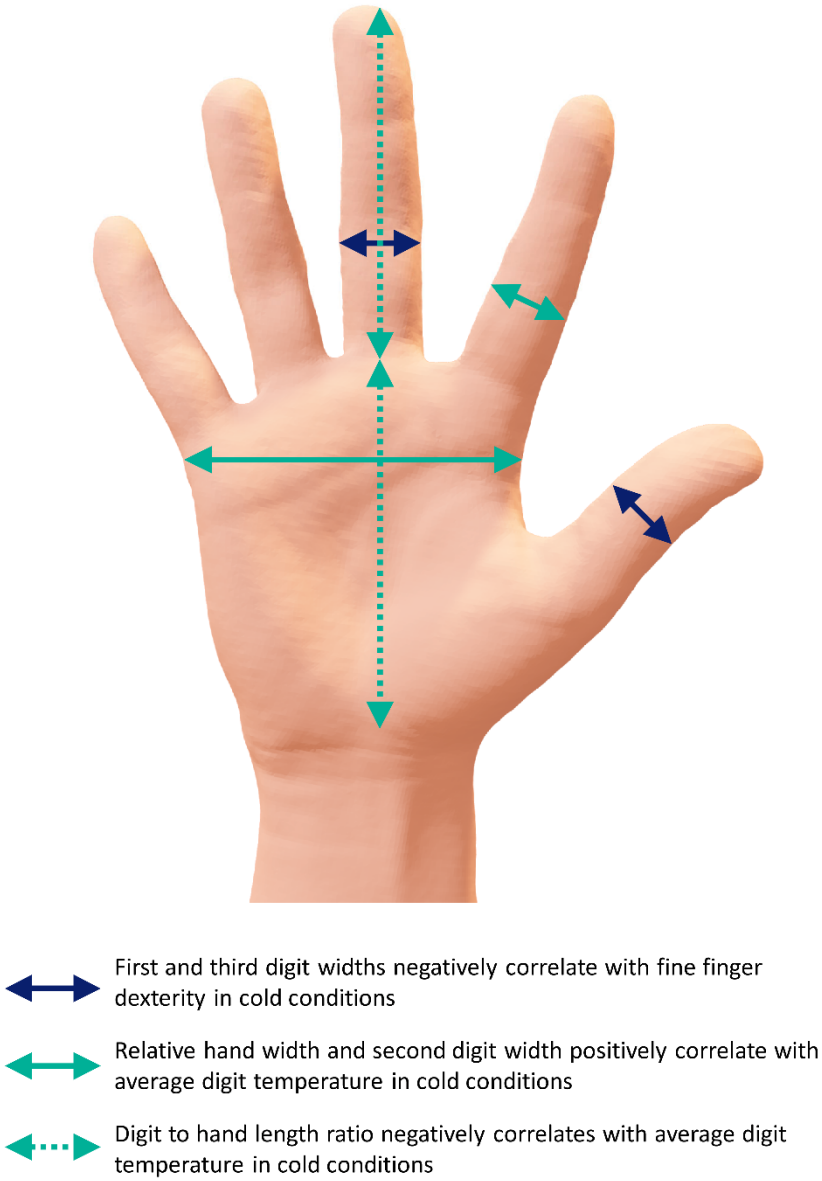


Figure 5.3 Diagram of which hand and digit dimensions associate with dexterity and thermoregulation based on results from the current study and Payne et al. (2018b).

Some individuals, irrespective of average digit temperature and digit width, in fact, increased in dexterity after the ice-water immersion. This may be due to an improvement over time with practice of the Purdue pegboard test. Whilst three practice runs were carried out as recommended (Gallus and Mathiowetz, 2003), some participants may still have improved after this practice period. Further investigation may be required to determine whether these cases are removed with further practice.

From an evolutionary perspective, the findings here indicate a trade-off in functions of the hand in cold conditions. Whilst dexterity may be compromised with wider digits, wide digits are likely to protect from cold injury, and thus may be more advantageous in the long term, over a short term compromise in fine finger dexterity. It is worth noting that the Purdue pegboard test is only one measure of dexterity, used to quantify fine finger dexterity (Yancosek and Howell, 2009), specifically, the completion of thumb-finger precision pinch grips in quick succession. This test does not measure other elements of dexterity, such as overall manual dexterity (any task which requires the coordination of the entire hand), hand steadiness, overall grip strength or grip sensitivity (Fleishman and Ellison, 1962). Indeed, all these elements of manual dexterity are compromised by lower temperatures (Teichner, 1957; Riley and Cochran, 1984; Heus et al., 1995; Daanen, 2009; Cheng et al., 2014; Cheung et al., 2016), but whether different hand or digit proportions affect these other elements of dexterity has yet to be investigated. Fine finger dexterity is representative of some essential survival tasks, such as lighting a fire, threading a needle, processing food, or utilising a fishing hook (Cheung, 2015). Past and present populations may have found such tasks challenging in cold conditions. Notably, some Arctic hunter-gatherer groups have markedly complex fishing and hunting technologies (Torrence, 2001; Read, 2012), which may be particularly challenging to create and operate in severe cold. As populations residing in cold regions have been found to have wider digits (specifically the

first and second metacarpals) (Lazenby and Smashnuk, 1999; Betti et al., 2015), these populations may have found fine finger dextrous tasks particularly challenging, given the results found here, whereby wide digits result in a greater compromise in fine finger dexterity. Digit width may well have compromised fine finger dexterity but may have been essential for optimising thermoregulation. However, it is also possible that the capacity for dextrous tasks may be maintained by vasoregulatory mechanisms, which are known to be enhanced in Arctic populations (Brown et al., 1953; Page and Brown, 1953; Meehan, 1955; Elsner et al., 1960), and fishermen operating in high latitude regions (LeBlanc et al., 1960; Steegmann, 1977), but this requires further investigation.

Based on the findings of the current study, it may be possible to infer potential cold-associated dexterity limitations in extinct hominins. Species with relatively wide digits may have significantly reduced fine finger dexterity in cold conditions. Neanderthals are considered to have highly robust phalanges (Musgrave, 1971), indicating they had wide digits, and thus potentially may have had reduced fine finger dexterity both in temperate and cold climates. Furthermore, Neanderthals are considered to have had hypertrophied hand musculature based on the increased projection of some carpal tubercles (Niewoehner, 2006), and prominent opponens pollicis crest (Trinkaus, 1983). This enhanced musculature may have impaired dexterity in cold conditions, as muscle contraction velocity and force reduces with decreasing temperature (Clarke et al., 1958). Further research is required to ascertain whether muscle hypertrophy does indeed significantly compromise dexterity in cold conditions.

5.4.1. Conclusion

The current study suggests that digit proportions influence dexterity in cold conditions; narrow fingers are advantageous at carrying out fine finger dexterity tasks after acute cold exposure. However, narrow digits compromise thermoregulation. As wider hand

proportions are found in cold-inhabiting populations, this may indicate that climate is the primary selective pressure for wide hand and digit morphology in cold conditions, despite the reduction in dexterity, as overall long-term function is better preserved. This could inform inferences about the hand morphology of extant and extinct hominin populations. Further research is required to ascertain the underlying physiological mechanism behind the relationship between fine finger dexterity in the cold and digit width, and whether this relationship is also seen for other manual dexterity tasks.

PART II – Field Investigation

Chapter 6

Thrifty Phenotype vs Cold Adaptation: Trade-offs in Upper Limb Proportions of Himalayan Populations of Nepal

This paper was accepted for publication in the Royal Society Open Science journal on 14 May 2018 (Payne et al., 2018d).

Objectives: The current study investigated whether relative upper limb proportions of Himalayan adults differ between highland and lowland populations, and whether cold adaptation or an energetic stress response relating to the thrifty phenotype hypothesis may be acting here.

Materials and Methods: Height, weight, humerus length, ulna length, hand length, and hand width were measured in Himalayan adults (n=254) from highland and lowland populations using standard methods.

Results: Relative to height, total upper limb and ulna lengths were significantly shorter in highlanders compared to lowlanders in both sexes, whilst hand and humerus length were not. Hand width did not significantly differ between populations.

Discussion: These results support the thrifty phenotype hypothesis, as hand and humerus proportions are conserved at the expense of the ulna. The reduction in relative ulna length could be attributed to cold adaptation, but the lack of difference between populations in both hand length and width indicate that cold adaptation is not shaping hands proportions in this case.

6.1. Introduction

Life at high altitude (>3000 metres) is associated with extreme environmental stresses (Morpurgo et al., 1976; Pawson, 1976; Moore et al., 1998; Moore, 2001; Beall, 2006, 2014; West et al., 2013; Bigham and Lee, 2014; Gilbert-Kawai et al., 2014). Hypoxia, one of the few environmental stresses that cannot be effectively buffered by cultural adaptation (Beall et al., 2012a), in combination with low ambient temperatures, a physically demanding lifestyle, and nutritional constraints create a multi-stress environment which is highly challenging to longer-term human occupation (Gilbert-Kawai et al., 2014). In order to deal with these stresses, high altitude populations such as Himalayan, Andean and Ethiopian groups have adapted, both genetically and developmentally, through multiple adaptive pathways (Pawson, 1976; Beall, 2006, 2014; West et al., 2013; Bigham and Lee, 2014; Gilbert-Kawai et al., 2014) (Table 6.1). Genetic changes affecting hypoxia-inducing factor pathways (Scheinfeldt et al., 2012; Bigham et al., 2013) have been identified in all three groups, in addition to genetic changes in oxygen sensing (Ge et al., 2015) in Himalayans and Andeans, and glucose and insulin sensing (Wang et al., 2011) in Himalayans, overall enabling efficient mitochondrial metabolism in hypoxic conditions (Horscroft et al., 2017). This evidence demonstrates that quantitatively different genotypes have developed in high altitude regions. Whilst high altitude populations have evolved efficient mechanisms for dealing with hypoxia, limited energy availability can often result in trade-offs during growth, creating a different phenotype from lowland populations (Pawson, 1977; Smith, 1997; Weitz et al., 2004; Bailey et al., 2007; Argnani et al., 2008; Moore et al., 2011; Pomeroy et al., 2012, 2013, 2014; Weitz and Garruto, 2015). Whilst it is often difficult to obtain lowland populations that are directly comparable to highland populations in terms of lifestyle, culture and genetics, proximate groups are often used to find the closest fit to comparable populations.

Table 6.1 List of traits found in high altitude populations (>3000m) compared to local lowland native groups

	High Altitude Region		
Trait	**Himalayas/ Tibet**	**Andes**	**Ethiopia**
Height	↓ (Pawson, 1976, 1977)	↓ (Beall, 2006)	↑ (Harrison et al., 1969)
Sitting Height	↑ (Tripathy and Gupta, 2007)	↑ (Trowbridge et al., 1987)	↑ (Clegg et al., 1972)
Relative zeugopod length	↓ (Bailey and Hu, 2002)	↓ (Pomeroy et al., 2012)	↓ (Clegg et al., 1972)
Fat mass	↓ (Boyer and Blume, 1984)	↓ (Haas et al., 1977)	↓ (Harrison et al., 1969)
Chest volume	↑ (Tripathy and Gupta, 2007)	↑ (Greksa, 1986)	↑ (Harrison et al., 1969)
Exhaled nitric oxide	↑ (Erzurum et al., 2007)	↑ (Beall et al., 2001)	↑ (Beall et al., 2012b)
Erythrocytosis	↔ (Beall, 2014)	↑ (Beall, 2014)	↔ (Xing et al., 2008)
Arterial O_2 concentration	↓ (Beall et al., 1997)	↑ (Beall et al., 1997)	↔ (Beall, 2006)
Altitude sickness with age	↑ (Xing et al., 2008)	↑ (Beall et al., 1992)	↔ (Xing et al., 2008)

↑ - Increase; ↓ - Decrease; ↔ - No difference; O_2 - Oxygen

6.1.1. Plastic Growth

Linear growth during infancy and childhood appears to be moderately reduced with increasing altitude in Andean and Himalayan populations relative to their lowland counterparts (Beall, 1981, 1984; Gupta and Basu, 1981; Argnani et al., 2008), likely due to developmental plasticity. This height deficit has been commonly attributed to hypoxic stress, whereby limited oxygen compromises growth (Bateson et al., 2004; Weinstein, 2005; Julian et al., 2007; Argnani et al., 2008; Moore et al., 2011; Pomeroy et al., 2013, 2014; Eichstaedt et al., 2015; Ge et al., 2015). However recent evidence suggests that oxygen saturation does not correlate with height in high altitude Andean populations, indicating that nutrition and socioeconomic factors may play a more important role in stunted growth patterns (Weitz et al., 2004; Pomeroy et al., 2013). Indeed, it is likely to be multiple high altitude-related stresses contributing to reduced growth in high altitude populations. Interestingly, Ethiopian highlanders are not reported to have reduced linear growth relative to their lowland counterparts (Harrison et al., 1969); in fact, highlanders have greater height than lowlanders, but this trend has been attributed to higher disease

prevalence in lowland populations, thus potentially causing another energetic demand on lowland populations that compromises linear growth.

Clarifying where in the body the reduction in growth occurs is a strong indicator of the reason behind reduced height. The most significant decrement in height relative to lowland populations occurs in tibial growth, whilst sitting height remains the same (Bailey and Hu, 2002; Bailey et al., 2007). The reduction in tibia length is mirrored by a reduction in radius length in some Andean populations (Pomeroy et al., 2012), although this currently remains untested in Himalayan populations. Pomeroy *et al.* speculated that their findings could be attributed to a developmentally plastic response relating to the thrifty phenotype hypothesis (Hales and Barker, 1992). Whilst the thrifty phenotype hypothesis originated to explain the association between poor nutrition during early life and susceptibility to type II diabetes mellitus, it has since been expanded upon to suggest that susceptibility to a range of chronic diseases could relate to selection for a thrifty growth trajectory during early life, if nutritional status changes between early life and adulthood (Barker et al., 2002; Wells, 2011). This concept of thrifty phenotypic plasticity under energetic stress may be extended to growth prioritisation of certain critical body elements, such as the brain, at the expense of the full growth of other organs; this concept is applied by Pomeroy *et al.* (2012), to explain the reduction in forearm and lower leg segments elements relative to hands and feet. The authors argued that this pattern preserved function in the hands and feet, and that this pattern was inconsistent with the alternative distal blood flow hypothesis (Lampl et al., 2003), which would predict a gradient of decreasing relative distal segment length with increased distance from the body as a result of progressively reduced nutrient availability. It remains untested whether the same pattern of relative size in different segments of the extremities is observed in high altitude Himalayans. Greater cold stress in the Himalayas may result in different limb proportions from those of Andeans.

6.1.2. Potential Cold Adaptation

Whilst both the Himalayas and the Andes have considerable local variation in temperature and humidity, high altitude populations in the Himalayas are exposed to lower temperatures on average compared to Andeans due to differences in latitude, topography, rainfall and ecology (Barry, 1992). The highland populations of Peru, Ecuador, and Bolivia, residing up to as high as 4500m above sea level, are likely to experience limited seasonality, but a significant range in diurnal temperature (Thomas and Winterhalder, 1976). During winter, inhabitants of the highest settlement in the Andes, La Rinconada in Peru, are exposed to annual minimum temperatures of approximately -20˚C (Merkel, 2016). Minimum temperatures are reported to be lower in some Himalayan settlements, such as Lo Manthang in Nepal, reaching below -30˚C in winter (Merkel, 2016; Vuillermoz, 2016). Whilst it is impossible to make generalisations about such vast and climatically diverse mountain ranges, extreme temperatures are probably the most influential as potential selection pressures. The lower minimum temperatures in some Himalayan settlements may be a greater selection pressure for good thermoregulation and minimising risk of cold injury, and thus thermal selection pressures may have shaped the limb morphology of Himalayan populations unlike other high altitude populations. Himalayan limb morphology may resemble the cold adapted patterns found in other populations exposed to low temperatures (Lazenby and Smashnuk, 1999; Betti et al., 2015), such as shorter and broader first and second metacarpals in individuals residing in cold climates than individuals from hot climates. These patterns found in metacarpal dimensions support Allen's rule (Allen, 1877), where appendage length is reduced and appendage breadth increased to reduce heat loss in a cold climate.

Thus, applying Allen's rule to predict limb proportions in Himalayan populations, we would expect them to have shorter and broader limbs to minimise heat loss. Minimising

heat loss would reduce energetic demands on the body from maintaining body temperature, which may well be selected for as energetic stress is already strong in these populations as a result of multiple altitude-related stresses. Furthermore, low temperatures would also put individuals at greater risk of cold injury in the extremities (Subedi et al., 2010; Moore and Semple, 2011). Although there are individually reported cases of Sherpas with frostbite (Subedi et al., 2010; Macdonald et al., 2015), they tend to have a lower incidence than recreational mountaineers, although this may be due to differences in behaviour (Takeoka et al., 1993; Maley et al., 2014). These findings suggest that Sherpa hands may be better adapted to life in cold conditions, but whether hand dimensions play a role remains untested. By measuring hand dimensions of a sample of Sherpas, it may be possible to infer whether both their absolute and relative hand dimensions are suited to heat preservation or not.

As the extremity proportions of permanent Himalayan populations remain poorly documented (Sloan and Masali, 1978; Gupta and Basu, 1981; Tripathy and Gupta, 2007), it is currently not possible to infer the key environmental stresses in Himalayan high altitude upper limb morphology and how the trade-off is balanced between dexterity and thermoregulation. Thus, the current study investigates the limb proportions of highland and lowland groups from the Himalayas to determine how the multi-stress environment of high altitude influences limb morphology.

6.2. Methods

6.2.1. Study Sample

The lowland population (n=71) was sampled from a migrant Tibetan community in Jawalakhel, Kathmandu, Nepal (1400 m above sea level, 27.6744° N, 85.3123° E; average minimum winter temperature= 3.1˚C (Merkel, 2016)). Whilst this population was located at moderate altitude, the significant impacts of altitude on the body are reported to only

emerge approximately 2000m+ above sea level (Young and Reeves, 2002), thus this community was considered suitable as a comparable lowland population. A Tibetan community was selected as they share common genetic ancestry with the highland population (Bhandari et al., 2015), and have similar diets and activity levels. Whilst Tibetan and Sherpa groups are still genetically distinct, Tibetans are the most closely genetically related to Sherpa, and therefore make the most suitable comparison group. The highland population (n=183) was sampled from several Sherpa communities in Namche Bazaar and surrounding villages, Nepal (3500m+ above sea level, 27.8069° N, 86.7140° E; average minimum winter temperature= -7.9˚C (Merkel, 2016)) (further details of the population can be found in Appendix 2). Each participant self-identified as Tibetan or Sherpa in the lowland and highland populations respectively, and evidence of birthplace was confirmed when possible through birth certificates or school records. A convenience sample of 254 participants between the age of 18 and 59 was measured. Convenience sampling was used for two reasons; due to the dispersed nature of many of the highland settlements, and the relatively low number of individuals of Tibetan origin in Kathmandu. Thus, sampling was limited to the groups that were easily accessible within the limited data collection time frame. Inevitably, there were likely sampling biases resulting from this form of data collection. The convenience sampling method may have resulted in differences in number of men and women between lowland and highland samples, based on who was available and willing to talk to investigators at the time of the study. As the lowland population were workers in the Jawalakhel community centre, only those relatively fit and healthy would have been sampled. Those from the Tibetan community who were able to get passports and work abroad, predominantly young men, would not be well represented in the lowland sample. Both highland and lowland samples were dependent upon those willing to cooperate with researchers, which may have also brought in an element of unknown bias.

6.2.2. Ethics Statement

Participation was unpaid and voluntary and the study was conducted according to accepted international ethical standards for research involving human subjects (Declaration of Helsinki) (World Medical Association, 2013). The study was approved by the Human Biology Research Ethics Committee at the University of Cambridge (HBREC.2016.22), and the Nepal Health Research Council (Reference Number: 1571) (ethics proposal and approvals can be found in Appendix 1). Written informed consent was obtained from all participants by signature, or fingerprint if not literate.

6.2.3. Anthropometry

Height was measured to the nearest mm using a Seca Leicester Portable Height Measure following standard protocols with participants dressed in light clothing and unshod (Moore, 2001; Beall, 2006). Weight was measured to the nearest 0.05 kg using SECA-807 weighing scales (Seca, Birmingham, United Kingdom). Upper limb segment measurements were taken using Trystom anthropometer A-226 (Trystom, spol s.r. o, Czech Republic). Both humerus and ulna length were measured following standard definitions (Lohman et al., 1988). Humerus length was measured from the lateral border of the acromion to the inferior extent of the olecranon (elbow flexed at 90 degrees), while ulna length was taken from the olecranon to the head of the styloid process. Hand dimensions were measured following definitions by Davies *et al.* (1980), with palm facing upwards, fingers and palm fully extended and hand flat, with dorsum of the hand resting on a horizontal surface. Hand length was measured from the level of the ulna styloid to the greatest extension of the middle finger perpendicular to the long axis of the hand. Hand width was measured as the linear distance between the radial side of the second metacarpophalangeal joint and the ulnar side of the fifth metacarpophalangeal joint

(Davies et al., 1980). Humerus, ulna, and hand lengths were summed to give total upper limb length.

6.2.4. Statistical Analysis

To take account of differences in body size, upper limb segments relative to height were compared between populations. Relative segment lengths were calculated as follows:

$$Relative\ segment\ length = \frac{Absolute\ segment\ length\ (cm)}{Height\ (cm)}$$

Both absolute and relative segment lengths were analysed using independent *t*-tests between the highland and lowland populations. To remove any sex differences, male and female data were analysed separately. Normality was tested using the Shapiro-Wilk test on all data. All statistical analysis was carried out using SPSS 25.0 for Windows.

6.3. Results

Table 6.2 Descriptive statistics of highland and lowland populations

	Female			Male		
	Lowland (n=42)	**Highland (n=48)**		**Lowland (n=29)**	**Highland (n=135)**	
	Mean (SD)	**Mean (SD)**	**Sig.**	**Mean (SD)**	**Mean (SD)**	**Sig.**
Height	154.1 (±5.7)	155.5 (±6.3)	p>0.05	168.2 (±7.0)	165.1 (±7.0) **	p<0.01
Total Arm Length	71.3 (±3.7)	70.0 (±3.3)	p>0.05	77.6 (±3.9)	74.6 (±3.8) **	p<0.01
Humerus Length	29.1 (±1.8)	29.0 (±2.0)	p>0.05	31.4 (±1.8)	30.3 (±2.1) **	p<0.01
Ulna Length	24.3 (±1.5)	23.2 (±1.4) **	p<0.01	26.8 (±1.7)	25.4 (±1.8) **	p<0.01
Hand Length	17.8 (±0.9)	17.7 (±0.9)	p>0.05	19.4 (±1.3)	18.9 (±0.1) *	p<0.05
Hand Width	9.2 (±0.5)	9.1 (±0.6)	p>0.05	10.2 (±0.7)	9.9 (±0.6)	p>0.05

All anthropometric variables were measured in cm. Total arm length includes humerus ulna and hand length
*Sig. = significance. *=p <0.05; **=p<0.01*

Absolute ulna length was significantly longer in lowlanders than in highlanders in both sexes (Table 6.2). In males, highlanders were significantly shorter in height, total

upper limb length, humerus length, ulna length and hand length. Absolute hand width did not significantly differ between populations in either sex.

Relative to height, total upper limb and ulna lengths were significantly shorter in highlanders compared to lowlanders in both sexes, whilst relative hand length and width and relative humerus length were not significantly different between the two populations (Figure 6.1: $p>0.05$ for both sexes).

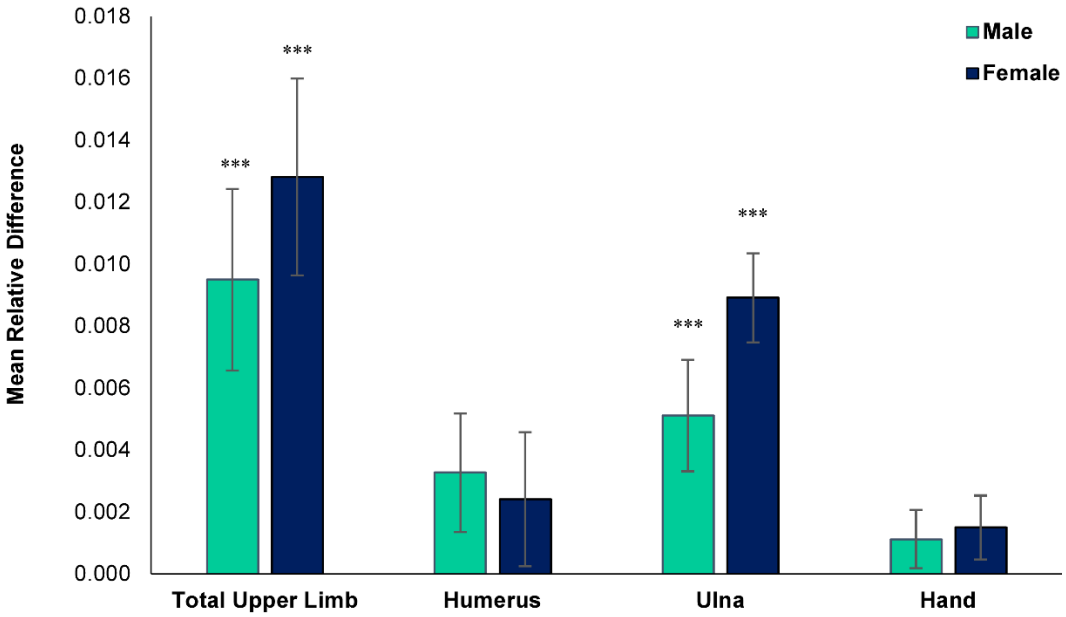


*Figure 6.1 Bar chart of mean difference in upper limb segment length relative to height between lowland and highland populations (Mean relative difference calculated as lowland relative mean – highland relative mean) *** = p<0.01*

6.4. Discussion

These results are consistent with previous findings in children from Andean populations (Pomeroy et al., 2012), as relative hand and humerus proportions are conserved at the expense of the ulna. This suggests that limb growth may respond to environmental stress in Himalayan populations in a similar way to that seen in Andean populations, and provides support for plasticity, possibly in the form of a thrifty phenotype

mechanism, in shaping limb segment proportions in the presence of high altitude stresses. Whilst the current study only investigated adults (aged 18-59), it indicates that the adult phenotype reflects the pattern which develops during childhood (Pomeroy et al., 2012), whereby relative ulna length is reduced whilst relative humerus and hand length are not.

The current study aligns with prior evidence of selective plastic growth under environmental stress (Bogin et al., 2002; Pomeroy et al., 2012), whereby certain limb segments, such as femur or humerus and hand, grow to near expected full length, whilst other segments, such as tibia or ulna, do not. No difference was found in relative hand length or width between the populations, indicating that no compromise in growth was made in hand dimensions. Relative ulna length was significantly shorter in highlanders relative to lowlanders, indicating reduced growth of this limb segment. Differences in altitude may result in this limb segment difference as limited oxygen availability may reduce growth in the highland population, as previously seen in other high altitude populations (Greksa, 1990; Bailey et al., 2007). However, this explanation is based on hypothetical assumptions relating to prioritisation of functional elements, and thus requires further investigation to fully understand the underlying mechanisms behind the limb segment pattern found here and elsewhere (Pawson, 1977; Beall, 1981; Singh et al., 1986; Bailey and Hu, 2002). The preservation of humerus length in the highland sample may result from the prioritisation of the upper arm segment for functional purposes, but could also occur due to morphological integration and regulation of this segment during development (Zakany and Duboule, 2007), limiting plastic responses to growth environment in the humerus.

The reduction in relative ulna length could be attributed to cold adaptation (Ruff, 1991; Wilberfoss, 2012), but the lack of difference between populations in both hand length and width indicate that cold adaptation is not shaping hand proportions in this case.

It is possible that the forearms, but not hand proportions, are shaped by climate; Steegmann (2007) suggested that extreme vasoconstriction in the hands as a response to cold may negate any effect of hand proportions, as hand temperature may reach close to the surrounding temperature, and thus little heat is transferred to the surroundings from the hand. This is supported by cold immersion tests, whereby heat flux from the hand is consistently lower than heat flux from the forearm, even when a temporary CIVD response occurs in the fingers (Wang et al., 2007). The forearm does not have such vasoregulatory responses (Rodriguez-Niedenfuhr et al., 2001; House and Tipton, 2002), and thus may be more susceptible to heat loss, and thus shortening of the zeugopod segment may have a significant effect on reducing energy expenditure via reduction in heat loss (Steegmann, 2007). The mechanism for this adaptive limb segment shortening in the presence of cold stress is unknown, but plasticity may play a role. It is well documented that temperature influences long bone elongation during postnatal development in several species, including mice (Sumner, 1909; Sundstroem, 1922; Ogle, 1934; Serrat et al., 2008, 2009), rats (Chevillard et al., 1963; Lee et al., 1969; Riesenfeld, 1973), rabbits (Ogle, 1933), and pigs (Weaver and Ingram, 1969). This plastic growth response to temperature may influence high altitude long bone proportions; however, this plasticity in response to temperature has yet to be investigated in humans.

The hand proportions measured in the current study do not appear to align with cold adaptation theory. This may be for several reasons. Firstly, cold stress may not be the dominant factor influencing limb proportions; maintenance of hand dimensions for dexterity may be acting here (Marzke and Marzke, 2000). Evidence in the skeletal record suggests that cold adaptation theory may explain patterns in digit proportions of high latitude-dwelling populations (Lazenby and Smashnuk, 1999; Betti et al., 2015), but may not be applicable to high altitude populations. The highland population in the current

study may not show cold adaptation patterns in the hands as they may not be exposed to extreme low temperatures as regularly or for such prolonged periods as populations at very high latitudes, and the high insolation of the Himalayas during the day may alleviate cold stress (Merkel, 2016; Vuillermoz, 2016). Alternatively, the results here may indicate that in Himalayan populations, temperature does not act on hand proportions through plastic mechanisms. As the lowland population had a shared genetic ancestry with the highland population (Bhandari et al., 2015), both populations may have the same genetic-based long term adaptations which shape the hands, which may or may not relate to cold adaptation. Finally, there could be other modifying factors here, such as the use of gloves or insulative clothing in highlanders to alleviate any cold stress effects, but this was not measured in the current study.

The results here do not support the distal blood flow hypothesis (Lampl et al., 2003), as the hand was not significantly reduced in length or width relative to the rest of the body in highlanders compared to lowlanders. This again aligns with findings from Andean populations (Pomeroy et al., 2012). However, this limb proportion pattern may indirectly be linked to differential blood supply to hand and forearm segments. When blood vessels are fully perfused, blood supply is greater in autopod segments than zeugopod segments, due to dense capillary networks in the hands and feet (Standring, 2008), where blood moves slowly and thus nutrient delivery is highly efficient. Even if there is significant vasoconstriction in the highland populations during cold exposure, there may still be sufficient nutrient delivery to the deep tissue and bones of the hands, ensuring essential bone development and regeneration (Tomlinson and Silva, 2013; Ramasamy et al., 2016). Whether vasoconstriction negates any effect of differential blood supply requires further investigation.

Although overall the diet and activity of the two populations were similar, there may have been some differences which were difficult to quantify. Lowland individuals self-reported a traditionally Tibetan diet but may also have had access to Westernised food as globalisation has increased the diversity of food products available in Kathmandu. Differences in activity may also have occurred; the women in both populations were homemakers and living relatively sedentary lifestyles; the men in the lowland population were factory workers, whilst the men in the highland population were porters. Whilst the men in both populations were manual labourers, energy expenditure of activity was not directly measured in this case, so any differences in activity were unknown. Previous work indicates a very high daily energy expenditure of highland porters (Malville et al., 2001); further investigation would be required to determine the daily energy expenditure of Jawalakhel factory workers.

The significant differences between males in all absolute variables other than hand width may be due to greater sensitivity to environmental stresses in males (Stinson, 1985). As five different variables show the same pattern between the male populations (height, total upper limb length, humerus length, ulna length, hand length), this is unlikely to be a chance outcome. Alternatively, confounding factors such as unknown differences in diet or activity, as discussed above, may result in differences in body form between highland and lowland males. Although there is a difference in sample size between males, there are no assumptions relating to sample size when applying the independent samples t-test, and thus differences in sample size should not have an effect. However, it is possible that the lack of differences identified in the female samples, other than the significant difference in relative ulna length, may result from a lack of power due to the relatively small sample sizes.

Although the absolute differences were greater in males, the differences in relative ulna length and total upper limb length were greater in females. This may indicate differential investment in segment lengths between the sexes during energetic stress. Reports from Himalayan communities in both Nepal (Madjdian and Bras, 2016; Nath, 2017), and India (Kshatriya and Acharya, 2016), have indicated that during childhood, girls suffer greater malnutrition than boys as a result of differential intra-household food allocation patterns. These findings, in conjunction with a strong association found between nutritional status and women's health markers, including body mass index, and stature (Smith, 1997), suggest that greater relative differences in ulna length and total upper limb length in women compared to men may be nutritionally founded. Alternatively, the greater deficit in height in highland males reduces the relative differences in male upper limb segment lengths, and thus the outcome of males having reduced relative differences in ulna length and total upper limb length may merely be a consequence of scaling. This outcome needs further investigation to determine why absolute differences between highland and lowland upper limb segment lengths are greater in males, but relative differences are greater in females.

6.4.1. Conclusion

In conclusion, the current study showed heterogeneous reductions in different upper limb segments in association with altitude-related stresses in Himalayan populations. Relative to height, total upper limb length was significantly shorter in highlanders than lowlanders, a difference driven largely by reduced ulna length. These results provide further support for the thrifty phenotype hypothesis, as hand dimensions are prioritised over other upper limb segments for their manipulative function. Cold adaptation patterns in the hand were not found in this study, indicating that other selection pressures dictate limb proportions in the Himalayan high altitude environment.

Chapter 7

Conclusion

The principal aims of this thesis were to assess whether hand proportions may be adapted to climate and to evaluate the implications of hand variation on thermoregulation and dexterity. Using a multidisciplinary approach, including *in vivo* laboratory investigations and an anthropometric field study, this work explored the potential factors shaping phenotypic variation in hand proportions. The laboratory investigations directly assessed the relationship between hand proportions and heat loss from the hand during brief cold exposure and the implications for dexterity, whilst acknowledging potential confounding factors relating to body size and body composition. The field study tested whether cold adaptation is observed in a population experiencing significant cold and energetic stress, or whether other selective pressures influence phenotypic variation in the hand in this case. The outcomes from each of the investigations are summarised below.

7.1. Summary of findings

The *in vivo* laboratory-based investigation detailed in Part I (Chapters 3-5) not only provided empirical support for the application of climate adaptation theory to the human hand, but also demonstrated the complexity of the relationships between heat loss from the hand, whole-body thermal balance, and dexterity. Firstly, the study demonstrated the importance of skeletal muscle mass in maintaining hand temperature during cold exposure. Absolute and relative muscle mass predicted heat loss from the hands in cold conditions, whilst weight, height, and fat mass did not. This indicates that thermogenesis in muscle may be more important than insulative fat in maintaining digit temperatures, as heat lost at the surface of the hand may be replaced more quickly with greater

thermogenesis from a larger muscle mass. This highlights the importance of body composition in thermoregulation of the extremities and has enabled whole-body factors to be taken into account in the study relating specifically to hand dimensions.

In light of the findings relating to whole-body thermoregulation, body size was accounted for when testing heat loss from the hand in relation to hand proportions. This study demonstrated that hand proportions do indeed influence heat loss from the hand. Wider hands with relatively short digits retained more heat than other hand proportions. This provided experimental support for climate adaptation theory, as the assumptions using thermodynamic principles to explain Allen's rule hold true, despite potential confounding factors such as body composition and vasoregulation.

In contrast, the dexterity segment of this investigation indicated that narrow digits are advantageous for maintaining dexterity on cold exposure, despite a compromise in digit temperature. As cold-inhabiting populations have wider hand and digit elements than those of tropical origin, this suggests that climate, rather than maintenance of dexterity, is the primary selective pressure in cold environments. This may indicate that ecogeographic patterns found in the extremities are primarily driven by cold adaptation, rather than heat adaptation (Ocobock, 2014).

Part II tested whether climate adaptation patterns in the hands are observable in an energetically stressed population. Between high altitude and low altitude populations of shared genetic ancestry in the Himalayas, relative hand proportions were not significantly different, but relative ulna length was, indicating that a thrifty phenotype mechanism shapes limb proportions at high altitude. This puts the *in vivo* laboratory investigation into perspective, as it demonstrates that energetic stress is the primary selective pressure on hand proportions in this case, rather than climate adaptation. Although climate adaptation

is supported by gradients in digit proportions with latitude (Lazenby and Smashnuk, 1999; Betti et al., 2015), high altitude populations do not follow patterns of climate adaptation.

7.1.1. Comparison between laboratory and field investigation

To consolidate the findings of the current thesis, and to appreciate the variation in hand proportions across both the laboratory and field investigations, Tukey's boxplots were generated to observe the range of both relative and absolute hand length and width variables, as well as height, from the European population (reported in Chapters 3 and 4), and the Himalayan populations (reported in Chapter 6) (Figure 7.1 and Figure 7.2). It should be noted that the laboratory investigation used 2D photocopy scans in order to obtain hand measurements, whilst the field investigation used an anthropometer to obtain measurements from participants directly. Whilst it has been established that photocopies yield lower values than direct measurements (Manning et al., 2005), the differences are on average less than 1mm, and thus a comparison between populations was considered acceptable here. When sexes were analysed separately, all variables were normally distributed within each sample, as assessed by the Shapiro-Wilk Test, aside from male relative hand length and widths which were approximately normally distributed based on Q-Q plots. One-way ANOVA was carried out on each variable to assess whether the differences demonstrated in the Tukey's boxplots were significant.

Relative to height, both hand length ($F_{2,149}$=73.76, p<0.01 for women, $F_{2,212}$=37.20, p<0.01 for men) and hand width ($F_{2,149}$=516.46, p<0.01 for women, $F_{2,212}$=326.75, p<0.01 for men) were significantly lower in the European population in comparison to both the Himalayan populations. On analysis of the absolute variables, height was significantly different in Europeans from the Himalayan groups ($F_{2,149}$=95.37, p<0.01 for women, $F_{2,212}$=108.81, p<0.01 for men). This height difference is likely to have contributed to the difference in relative hand length and hand width. Absolute hand length was found to be

significantly different between Europeans and Himalayans in men ($F_{2,212}$=16.19, p<0.01), but not in women ($F_{2,149}$=0.96, p>0.05), whilst absolute hand width was significantly different in both sexes ($F_{2,149}$=222.07, p<0.01 for women, $F_{2,212}$=134.34, p<0.01 for men).

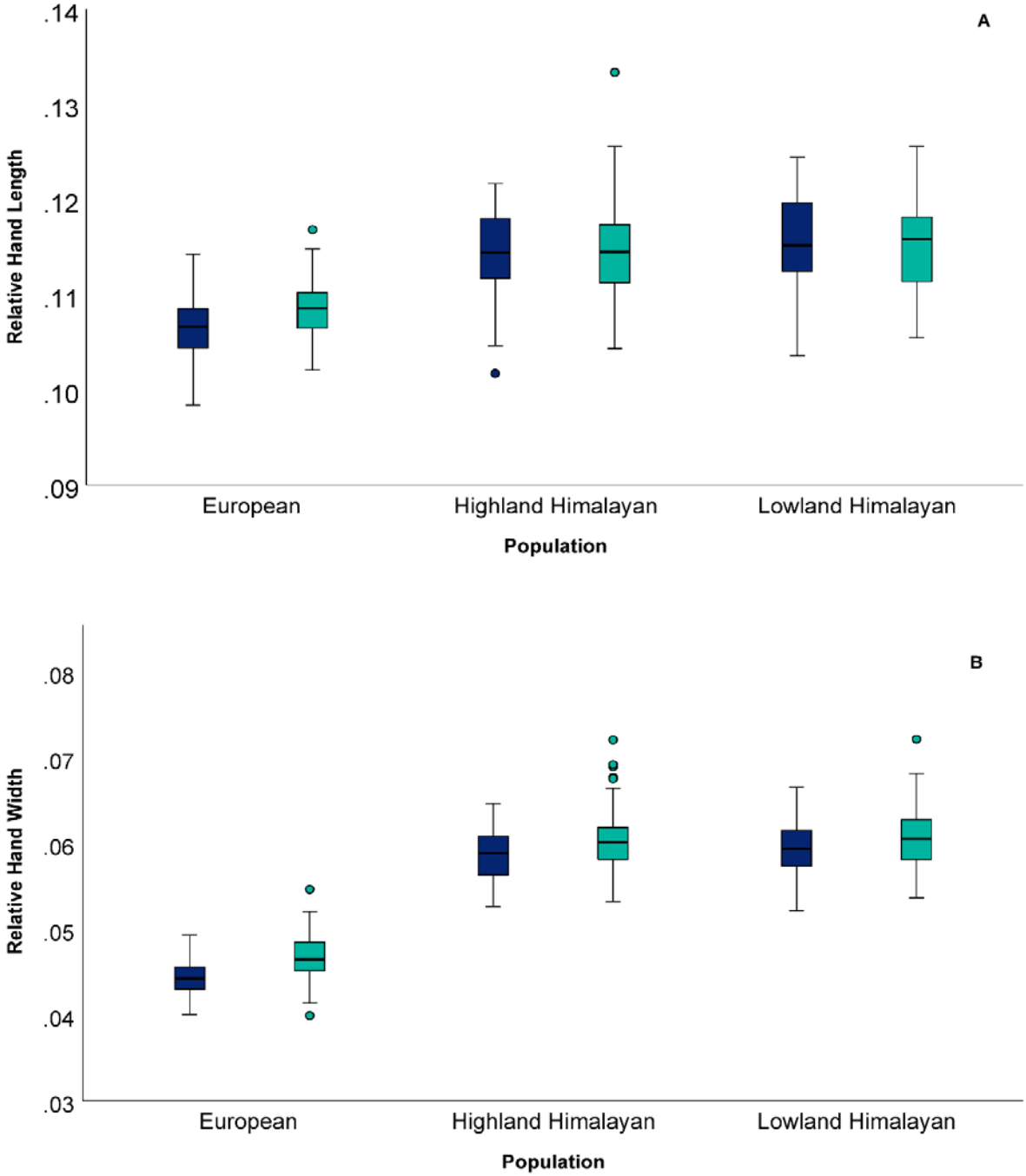


Figure 7.1 Tukey Boxplots showing differences between the populations from the laboratory study (Chapters 3 & 4 – European), and the highland and lowland Himalayan populations (Chapter 6) ; each box represents the respective interquartile range (IQR), whiskers represent the lowest value still found within 1.5 IQR of the lower and upper quartiles. Blue: female, Green: male. A. Differences in hand length relative to height. B. Differences in hand width relative to height.

The significant height differences are likely to be genetically founded, as the European sample and the two Himalayan groups are relatively genetically distant (Arciero et al., 2018). However, the environment may also have an influence on the height differences here. Developmental and childhood growth environments are likely to be different between these populations, in terms of nutrition, disease burden, oxygen availability, physical activity, and other unknown factors (Wells, 2007; Wang et al., 2016). This pattern in height differences between Himalayan populations and Europeans is well reported (Pawson, 1977; Argnani et al., 2008; Weitz and Garruto, 2015). The small difference in absolute hand length between men, and no difference in women, may indicate that hand length growth is not plastic, but relatively resilient to environmental stress during early growth and development (Holliday and Ruff, 2001), or that hand length is strongly morphologically integrated with the feet (Rolian, 2009).

Absolute hand width was notably different between Europeans and the two Himalayan groups. Similar to height, hand width could have a genetic basis (Wray, 2007; Carroll, 2008). Alternatively, differences in manual labour between these groups may also have contributed to the differences in hand width, as frequent manual activities may have cause greater musculature to develop in the palms (Okunribido, 2000; Vsnapuu and Jurimae, 2008; Fallahi and Jadidian, 2011). Both Himalayan groups had a physically active lifestyle that regularly used the hands, either through heavy lifting as porters, or through packing in the Jawalakhel centre. Whilst many of the participants in the laboratory study actively took part in sport, it is unlikely that they will have reached the same levels of manual activity as the Himalayan groups. Whether the differences between the groups stem from genetic or environmental causes is unknown, but the findings from this comparison in hand proportions between the laboratory and field investigations allow further reflection on the results from the previous chapters.

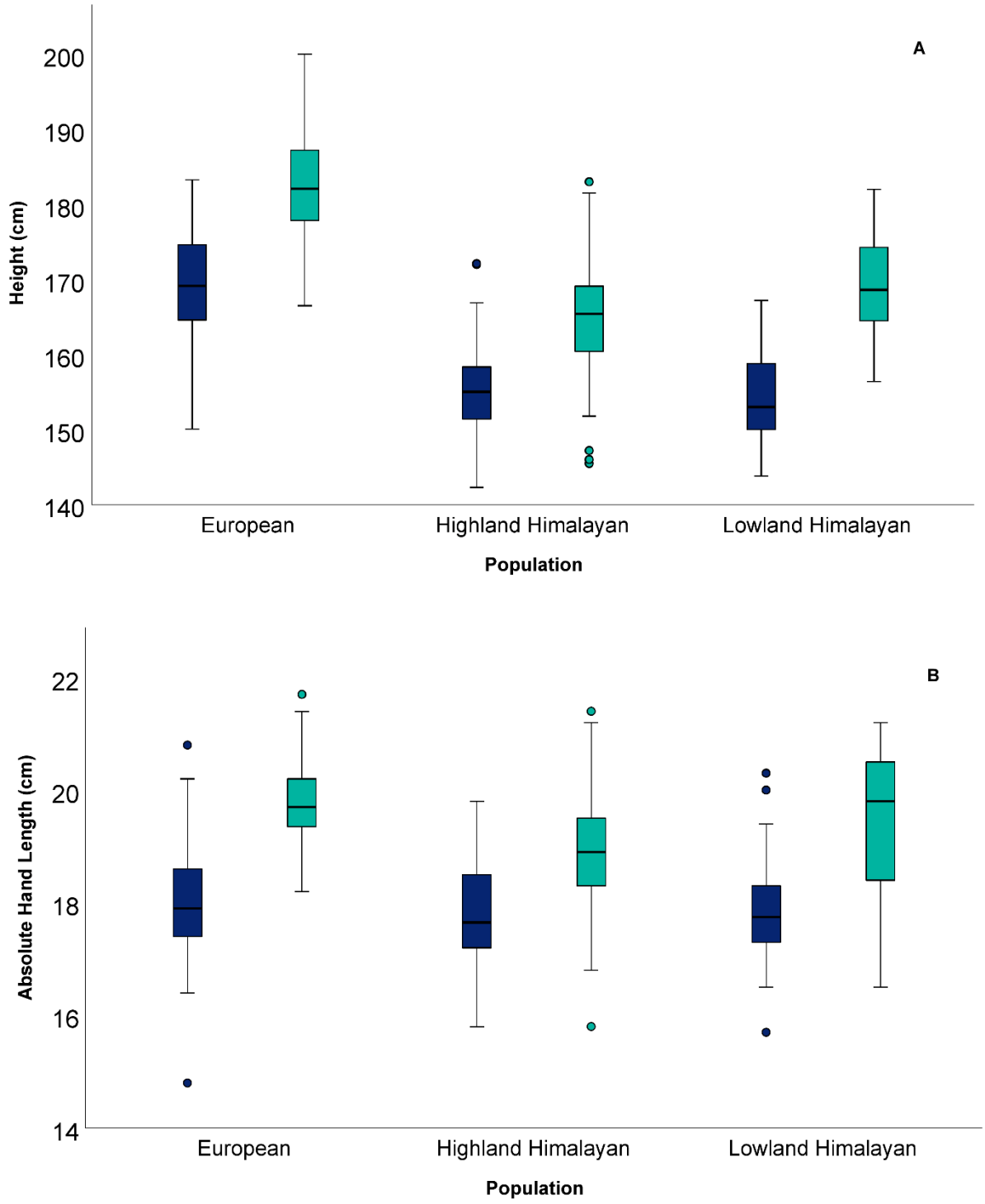

A
Height (cm)
200
190
180
170
160
150
140
European
Highland Himalayan
Lowland Himalayan
Population
B
Absolute Hand Length (cm)
22
20
18
16
14
European
Highland Himalayan
Lowland Himalayan
Population

Figure 7.2

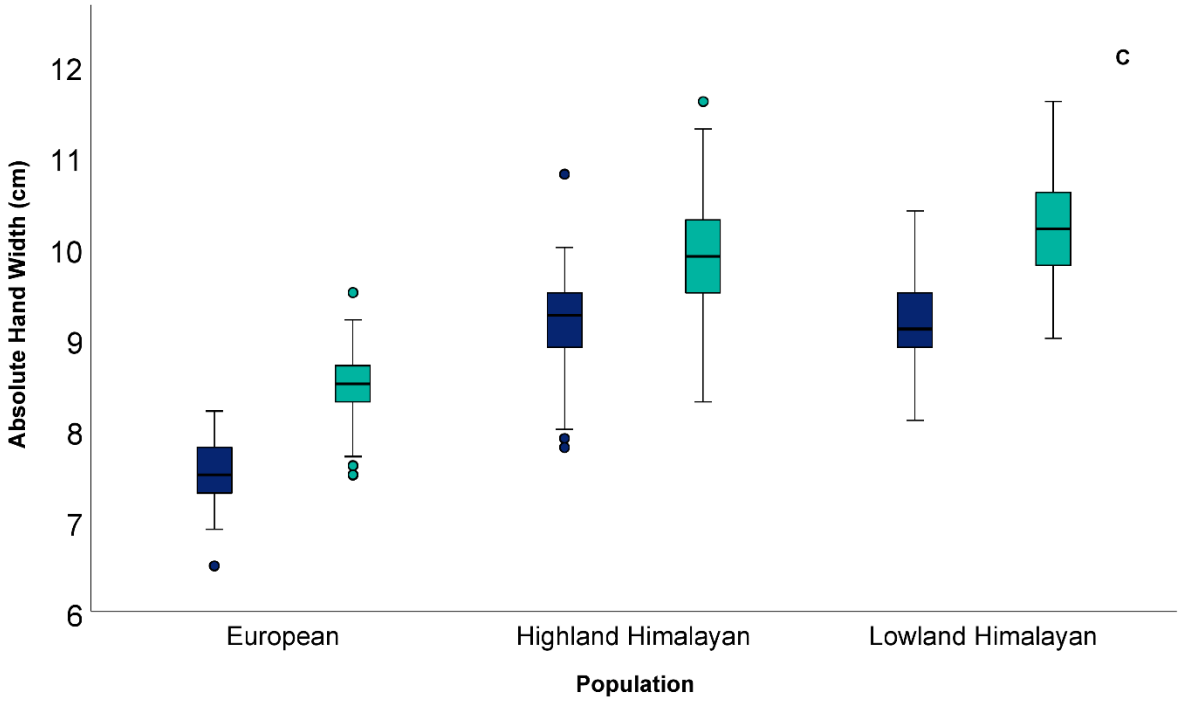


Figure 7.2 Tukey Boxplots showing differences between the populations from the laboratory study (Chapters 3 & 4 – European), and the highland and lowland Himalayan populations (Chapter 6); each box represents the respective interquartile range (IQR), whiskers represent the lowest value still found within 1.5 IQR of the lower and upper quartiles. Blue: female, Green: male. A. Differences in height. B. Differences in absolute hand length. C. Differences in absolute hand width.

The significant difference in both relative and absolute hand width between the laboratory sample and the field sample was particularly interesting, as whilst there was no difference between the highland and lowland samples seen in Chapter 6, it was evident that both groups have significantly wider hands than those of Europeans, despite being significantly shorter in height. As relative hand width was shown to predict average digit temperature after immersion in Chapter 4, this would indicate that Himalayan groups may retain higher hand temperatures on cold exposure than Europeans on average, as indicated in previous research (Little and Hanna, 1977; Mathew et al., 1979; Daanen and van Ruiten, 2000). The much smaller difference in hand length in men, and no difference in women, between the Europeans and both Himalayan samples was reflected in the little variation

seen in absolute hand length in Chapter 4 and Chapter 6, and again supports the idea of hand length being constrained by other factors, such as function or integration (Lemelin and Schmitt, 2016; Rolian, 2016). Considering how hand length and hand width vary across the populations studied here provides a broader context for assessing the implications of the results from both the laboratory and field study.

7.2. Implications for climate adaptation theory

The thermoregulatory role of limb proportions in climate adaptation has long been entrenched in anthropological theory, yet has not been experimentally validated (Steegmann, 2007). This research provides empirical evidence indicating that ecogeographical patterns found in humans could be attributed to cold adaptation (Allen, 1877; Ruff, 1994; Lazenby and Smashnuk, 1999; Betti et al., 2015), based on *in vivo* heat loss patterns seen here. Prior to this research, the key assumption surrounding climate adaptation theory, whereby thermoregulatory capacity is directly proportional to surface area-to-volume ratio of the body, did not account for differences in vasoregulation across the body or in the extremities. Previous research had demonstrated that heat loss significantly varied across different areas on the skin as a result of vasoconstriction from long-term full-body immersion, the torso losing approximately 24 Watts compared to the hand losing only 1.5 Watts (Wade et al., 1979). Despite vasoregulatory mechanisms, however, the current research demonstrated that hand proportions play a role in differential heat loss from the hand.

The current work also stresses the value of thermogenic tissue in thermoregulation, and that body size itself has minimal effect on hand temperature under cold stress. This aligns with whole-body immersion experiments, which observed that surface area-to-volume ratio of the body had little effect on core temperature and skin temperature regulation, but body composition plays a significant role (Sloan and Keatinge, 1973; Toner

and McArdle, 1988; Glickman-Weiss et al., 1991, 1993). Muscle appears to be essential for generating heat, as demonstrated by the high muscle mass of cold-inhabiting groups, although this may also result from a physically demanding lifestyle (Shephard et al., 1973). The outdated concept that white adipose tissue is the primary thermoregulatory tissue is further refuted here; previous experiments have demonstrated that most insulation comes from fat-free mass (Rennie, 1988), and suggests that white adipose tissue has not been selected for its insulative properties, but its energy storage capacity (Pond, 1998). Our changing understanding of human thermoregulation increasingly highlights the importance of metabolic adaptations, from evidence of increased metabolic rates in cold-dwelling populations (Leonard et al., 2005; Snodgrass et al., 2005), and also the presence of thermogenic brown adipose tissue among adults susceptible to heat loss (Nedergaard et al., 2007; Cypess et al., 2009).

It is worth noting that climate adaptation theory relating to limb proportions still has a key assumption which remains untested (Steegmann, 2007). If ecogeographic patterns seen in limb proportions are indeed adaptive, this would mean that the difference between having "optimised" and "non-optimised" limb proportions would have a significant impact on fertility or mortality (Mazess, 1975). Whilst it would not be feasible to test this empirically, it is important to acknowledge that there is still an untested assumption here that surrounds climate adaptation theory.

Furthermore, these adaptation theories need to be put into context with the range of adaptive behaviours which minimise heat loss. Access to shelter, limited outdoor activity, and the ability to make and wear clothing will act as significant buffers against the cold (Gilligan, 2010). In industrialised societies, this may largely negate the need for efficient physiological thermoregulation under cold stress. Even in human groups living in non-industrialised settings, behavioural thermoregulatory adaptations are more likely to

influence heat loss prevention, and ultimately survival, than biological adaptations (Steegmann, 2007). However, even with the development of clothing and shelter, the hands are regularly exposed when carrying out dextrous tasks in cold environments (Van Dilla et al., 1949; Daanen, 2009a), and thus optimal thermoregulation in the hands may still be an important selective pressure.

Not only does cold adaptation theory have to be put into context with behavioural adaptations, but also the many other forces acting to shape limb proportions. The field study demonstrated that energetic stress is the dominant influence in shaping limb proportions in Himalayan populations (Payne et al., 2018d), rather than cold stress. Whilst a considerable amount of literature is devoted to cold adaptation theory (Ruff, 1994; Holliday, 1997b; Steegmann, 2007; Tilkens et al., 2007; Foster and Collard, 2013; Roseman and Auerbach, 2015; Savell et al., 2016), the current field research demonstrates that ideas on climate adaptation may only be applicable when considering populations which are not under severe energetic stress. Not only will energy availability during growth influence limb proportions, but other factors, such as biomechanics and function (Kivell, 2015), and morphological integration (Rolian, 2009, 2016; Rolian et al., 2010), will shape the upper limb. Recent morphospace modelling shows that the human hand does not equate to the theoretical optimum of an anthropoid hand for manipulation (Hu et al., 2018), indicating that hand morphology is constrained by other factors, such as evolutionary history. Thus, a holistic systems biology approach may be useful when investigating phenotypic variation seen in human hands, and the body in general. This would also be of particular importance for understanding the evolution of hominin limb proportions.

7.2.1. Interpreting hominin morphology

The results presented in this thesis could provide useful context for the interpretation of the morphology of hominin remains and potential climate adaptation. For

example, as discussed in Chapter 5 , this could shed light on the perception of Neanderthal morphology as "cold-adapted" (Trinkaus, 1981; Ruff, 1994; Holliday, 1997b). Firstly, observing metacarpal morphology, Neanderthals tend to have longer palms relative to their digits (Musgrave, 1971; Mersey et al., 2013). This would indicate that their hands may have been well-suited to maintaining digit temperatures in cold conditions. This may be further enhanced by the significant body musculature traditionally associated with Neanderthal anatomy (Holliday, 1997b). This high relative muscle mass may also have supported warmer digit temperatures in cold conditions. However, the increased robusticity of the carpals, metacarpals, and phalanges (Trinkaus, 1983; Niewoehner, 2006), and evidence for well-developed digit flexor tendons (Kivell et al., 2018), indicate wider digits from greater soft tissue mass which would impair fine finger dexterity in cold conditions, based on the findings in the current thesis. Although not all Neanderthal populations would have been exposed to significant cold (Krause et al., 2007; Hublin and Roebroeks, 2009), the generalised robusticity of Neanderthal morphology indicates that they would have been well-suited to maintaining hand temperatures in cold conditions. As discussed previously, it is not possible to ascertain whether such traits have definitively been selected for thermoregulation, as other factors such as biomechanics and energetic stress are also likely to have shaped Neanderthal limbs.

The findings from the current thesis could be used to make inferences about the thermoregulatory implications of the hands in other fossil species with relatively intact hand remains. Near complete hand specimens such as those of *Homo naledi* (Kivell et al., 2015) and *Australopithecus sediba* (Kivell et al., 2011), with their mosaic of ancestral and derived features, would be interesting, albeit challenging, to place in a climatic context. However, the lack of secure attribution of many hand specimens to a given species limits

the extent of interpretation of the hand morphology and its thermoregulatory capacity in extinct hominins (Richmond et al., 2016).

7.2.2. Health and safety implications

The results here may be informative for individuals working or living in cold conditions, as those with phenotypic traits associated with lower average digit temperatures should take particular caution to monitor digit temperatures (Goldman, 1970; Hamlet, 1988; Valnicek et al., 1993). Individuals exposed to cold in the long term may be at risk of a permanent cold injury which would be detrimental to dexterity, as well as compromising quality of life, and potentially leading to more serious health problems as a result of post-injury infection (Golant et al., 2008; Makinen et al., 2009; Saemi et al., 2009). For example, occupational cold injury rates in military personnel undergoing winter mountain training exercises can be up to 12% (Reynolds et al., 2000). These injury rates could be reduced by identifying and monitoring digit temperatures of individuals with low relative muscle mass, or narrow hands and long fingers, to ensure that individuals who have morphologies associated with lower average digit temperatures do not develop cold injuries. Those at potential occupational risk include military personnel operating in cold environments (Oksa et al., 2006; Brändström et al., 2008), individuals involved in snow and ice sports (Johnson et al., 2007; Schindera et al., 2018), or those working with refrigerated or frozen goods (LeBlanc et al., 1960; Nelms and Soper, 1962; Enander et al., 1980; LeBlanc, 1988). Others may be at risk of heat loss as a result of their relatively low muscle mass, in particular, the elderly, with increasing muscular atrophy and reduced temperature perception (Guergova and Dufour, 2011). Individuals with relatively narrow hands and long fingers relative to palms may also be at greater risk of frostbite, as a result of predicted lower average digit temperatures in cold conditions. Also, children, having a very high surface area-to-volume ratio of their hands, may therefore be at greater risk, although

their resting metabolic rates tend to be higher compared to adults (Holliday, 1971), which may negate any influence of surface area-to-volume ratio, as heightened metabolic rate is seen to be a thermoregulatory advantage (Leonard et al., 2005; Snodgrass et al., 2005; Hancock et al., 2008; Castellani and Young, 2016). Overall, this study has a wide range of health and safety implications for a range of human groups.

7.3. Limitations and future directions

7.3.1. Quantifying vasoregulation

The current study did not quantify vasoregulation when measuring factors influencing heat loss from the hands. This would be considered a key limitation, as vasoregulation is known to significantly affect heat flux from the surface of the skin (Sendowski et al., 1997; Daanen, 2003; Merla et al., 2010; Cheung and Daanen, 2012; González-Alonso, 2014; Taylor, 2014; Cheung, 2015; Neves et al., 2015; Walløe and Walløe, 2016). The decision was made not to measure vasoregulation, as the application of Doppler-flow techniques to the protocol for the *in vivo* investigation would have been impractical and would likely have produced a high error rate in measurement, for several reasons. Firstly, there is significant variation in blood flow to different skin regions across the hand and arm, even with very close proximity (Tur et al., 1983; Sundberg, 1984), which would result in a high error rate when repositioning the Doppler probe after immersion tests (Agner and Serup, 1990; Braverman et al., 1990; Bircher et al., 1994). Furthermore, motion artefact noise using the Doppler method is a frequent limitation in experiments where the Doppler probe has to be moved, which would be inevitable between pre-immersion and post-immersion testing (Leahy et al., 1999). Variable moisturisation of the area will also affect the accuracy of the measurement, which would have been a particular issue, as hands were required to remain dry for more reliable readings of temperature using the thermal imaging camera, and thus liquid could not be used for a Doppler method

(Buraczewska et al., 2007). The consistency of measurement would also have proved a challenge as pressure and repeatability of finding the exact same position is known to affect this (Timmers et al., 2005; Cracowski et al., 2006). As a result of the high error rate which these factors would have produced, it was decided that vasoregulation would not be quantified in the current study. To ensure that the lack of measurement of vasoregulation did not impinge on testing the primary hypothesis, regression models were used so that vasoregulation could contribute to the unknown variation aspect of the models.

Increasingly, Doppler-flow technology is being developed to improve reliability in medical settings for measuring blood flow (Yvonne-Tee et al., 2005). As a result, this may in future provide an avenue for further research to determine the extent of vasoregulatory influence on heat loss and whether this interacts with body size, body composition, or hand proportions. As muscularity of limb elements is known to influence the size of arteries, this may in turn influence the extent of vasoconstriction and vasodilatation in response to cold exposure.

7.3.2. The diversity of the study sample

For the current laboratory study, the participants were of self-identified European origin. This was to minimise variation in homeostatic thermoregulatory responses which are associated with ethnicity (Farnell et al., 2008; Lee et al., 2013; Maley et al., 2014; Cheung, 2015). However, this means that the current study is not representative for the entirety of the human population, as variation in physiological responses to cold may negate any differences in hand proportions. A broader sampling approach across a range of ethnicities in future research may provide a more representative picture of the influence of human hand proportions on thermoregulation.

7.3.3. Heat loss in hot and humid conditions

The current study focused on heat loss in cold conditions. However, the role of hand surface area-to-volume ratio in hot or humid conditions is relatively under-studied, despite the diverse array of thermoregulatory adaptations attuned for excess heat loss in the hand (Chapter 1, Figure 1.1). As the majority of human evolution occurred in the tropics, heat loss should be well regulated, but determining whether the surface area-to-volume ratio of the hand plays a role in protecting the body from heat stress has yet to be clarified. Carrying out a test to determine whether hand proportions affect heat loss from the hands in hot conditions will further test the applicability of climate adaptation theory to the hands. It has been argued that humans may be better adapted to heat selection pressures than cold (Ocobock, 2014), but whether this relates to hand proportions remains understudied. Furthermore, humans are exposed to a wide range of climates of varying humidity; as the hand has the highest number of sweat glands per cm^2 on the body (Taylor and Machado-Moreira, 2013), an investigation into variation in hand-specific sweating rates across the globe may also be informative for understanding adaptation and physiological acclimatisation to specific climates.

7.3.4. Heat loss from the feet

Although the hands and feet are considered to be tightly morphologically integrated (Rolian, 2009; Rolian et al., 2010), evidence shows that this may not be the case for their physiological thermoregulatory responses to cold (Norrbrand et al., 2017). There is no association between hand and foot temperatures during cold stress and rewarming, and overall toe temperatures appear to be significantly lower than fingers both at room temperature and during cold stress. Investigating whether foot and toe proportions influence temperature in this case would provide an interesting future investigation to parallel the current study. Temperature decrease within the foot is associated with reduced

plantar sensation (Eils et al., 2004), altered muscle activity, and a slower, less efficient gait (Hohne et al., 2012; Zhang and Li, 2013), which may have interesting health and safety implications. Whether certain foot dimensions reduce this loss of plantar sensation and altered gait may inform interpretations of gait mechanics in different environments.

7.4. Concluding remarks

The methodology and results of this thesis are unique and readdress questions left unanswered in the field of human climate adaptation (Steegmann, 2007). Assumptions about the adaptive role of surface area-to-volume ratio have been established in anthropology with lack of experimental validation. This research is the first to provide empirical evidence that there is a relationship between hand and digit proportions, and heat loss from the hand. Furthermore, this research demonstrated the potential trade-off in hand proportions between thermoregulation and dexterity in cold conditions. These relationships between heat loss, hand proportions, and dexterity should be considered in light of whole-body traits, as this research demonstrates the significant influence that skeletal muscle mass has on thermoregulation on extremity temperature due to its powerful thermogenic properties. Associations between heat loss and hand proportions should also be put into a broader evolutionary context; whilst these results support the underlying assumptions behind cold adaptation theory, the field study of limb proportions in Himalayan groups demonstrates that energetic stress is the dominant influence on phenotypic variation in hand proportions over cold stress. The results presented here provide the foundation for further work unifying thermoregulation and phenotypic variation in the hand and the human body as a whole.

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Appendix 1 – Ethics Summary

The letter below demonstrates receipt of ethical approval for the laboratory and field investigations given by the Human Biological Research Ethics Committee at the University of Cambridge. Pages 144-165 detail the form submitted for ethical approval.

UNIVERSITY OF CAMBRIDGE
Human Biology Research Ethics Committee

Dr J Stock

I am pleased to let you know that the Human Biology Research Ethics Committee has considered your research project 'How does phenotype affect heat loss and dexterity?' and has agreed to give ethical approval.

The Committee attaches certain standard conditions to all ethical approval. These are:

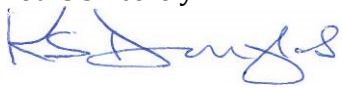
(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent correspondence concerning this application for ethical approval);

(b) that if the procedures used in the research project should change or the project itself should be changed you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;

(c) that if the employment or departmental affiliation of the staff should change you should notify us of that fact.

The Committee also asks that you inform members of any unexpected ethical issues. If you will let me know that you are able to accept these conditions, I will record that you have been given ethical approval.

Yours sincerely



Karen Douglas

17 Mill Lane
Cambridge CB2 IRX
Tel: 01223 766894

Ethics Application for both laboratory and field investigations

COUNCIL OF THE SCHOOL OF THE BIOLOGICAL SCIENCES
Human Biology Research Ethics Committee

Question 1: Title of the study
How does phenotype affect heat loss and dexterity?
Question 2: Primary applicant
Dr Jay Stock, University Reader Division of Biological Anthropology, Department of Archaeology and Anthropology, Pembroke Street, Cambridge, CB2 3DZ
Question 3: Co-applicants
Stephanie Payne, Probationary PhD Candidate Division of Biological Anthropology, Department of Archaeology and Anthropology, Pembroke Street, Cambridge, CB2 3DZ
Question 4: Corresponding applicant
Stephanie Payne (sp627@cam.ac.uk)
Question 5: In which Department(s) or Research Unit(s) will the study take place?
UK Laboratory Study Procedure – PAVE Imaging and Performance Laboratory, Division of Biological Anthropology, Department of Archaeology and Anthropology, Pembroke Street, Cambridge, CB2 3DZ Nepal Field Investigation – Namche Bazaar and Sagarmartha National Park, Solukhumbu District, Nepal, and Jawalakhel Tibetan Community Centre, Kathmandu, Nepal Storage and Analysis of Data from UK and Nepal - Division of Biological Anthropology, Department of Archaeology and Anthropology, Pembroke Street, Cambridge, CB2 3DZ
Question 6: What are the start and end dates of the study?
UK Laboratory Investigation – October 2016-April 2018 Nepal Field Investigation – 26th March- 21st April 2017
Question 7: Briefly describe the purpose and rationale of the research

This research will investigate how phenotypic variation influences heat loss from the hands and its relationship with manual dexterity. Human manual dexterity has enabled us to inhabit a wide range of ecological niches (Wells and Stock, 2007), by allowing us to manipulate our environment with highly dexterous hands (Marzke, 1971; Marzke and Marzke, 2000; Kivell, 2015). Traditionally, anthropological research has only focused on the early anatomical changes in the hands to facilitate basic tool use (Marzke, 1971; Wiesendanger, 1999; Marzke and Marzke, 2000; Churchill, 2001; Almécija et al., 2015; Heldstab et al., 2016), yet the refinement and optimisation of modern human hand traits remains entirely unexplored. Our hands are one of the most highly specialised structures in the human body (Boesch and Boesch, 1993; Marzke, 1997), not only as manipulative appendages, but also as dynamic thermoregulators (Taylor, 2014). The trade-off between these highly specialised traits remains poorly understood (Schiefer et al., 1984; Havenith et al., 1995; Heus et al., 1995; Daanen, 2009). This research will thoroughly investigate the interaction between the manipulative and thermoregulatory functions of the hands, and whether this interaction varies significantly in different hand proportions (Jay and Havenith, 2004; Daanen, 2009). Variation in hand proportions among human populations has been attributed to climate adaptation (Betti et al., 2015), but this theory has not been tested *in vivo.* This research will investigate whether hand proportions influence heat flux in real time, and whether certain proportions better preserve functionality under thermal stress, or whether dynamic thermoregulatory vasomotor responses can alleviate any effects that proportions have on heat flux from the extremities (Daanen, 1997; Daanen and van der Struijs, 2005; Cheung and Daanen, 2012). Testing hand proportions and responses during immersion-relate cold stress, and exercise-related heat stress will allow us to better understand the evolutionary trade-offs between thermoregulation, acclimatisation, function and energetic stresses in shaping human hands. Furthermore, by taking into account other body proportions, environmental conditions, and lifestyle factors, we can gain a more nuanced understanding of the origin of variation in human hand proportions. By quantifying hand proportions of populations exposed to extreme environmental conditions, such as cold and hypoxia, we can determine whether these energetic stresses also play a role in shaping human hands.

Laboratory research questions:

Do changes in hand temperature as a result of heating or cooling associate with:

- hand dimensions (length, breadth, estimated surface area, estimated volume),
- body size estimates
- body temperature
- dexterity

Do any of these variables correlate with one another?

Field research questions:

Is there phenotypic variation in upper limb proportions between highland and lowland populations in the Himalayas?

Do any differences in body proportions and lifestyle factors support:

- The cold adaptation hypothesis (Trinkaus, 1981)
- The distal blood flow hypothesis (Lampl et al., 2003)

Question 8: Who is funding the costs of the study?

Trinity Hall Graduate Research Studentship, Trinity Hall, Cambridge
The European Research Council - Covent Garden, Place Charles Rogier 16, 1210 Saint-Josse-ten-Noode (Brussels), Belgium
British Association of Biological Anthropology and Osteoarchaeology - Bournemouth University
Faculty Science and Technology, Dept. of Archaeology, Anthropology and Forensic Science
Christchurch House, Talbot Campus, Fern Barrow, Poole, Dorset, BH12 5BB
Sigma Xi The Scientific Research Society - 3200 East NC Highway 54, Research Triangle Park, NC 27709
National Geographic Society – Headquarters, National Geographic, 1145 17th Street N.W., Washington, D.C. 20036-4688

Question 9: Describe the methods and procedures of the study

Full details for all the investigations are detailed in the accompanying protocol of the UK Laboratory Investigation and the Nepal Field Investigation. A summary is found here-
UK Laboratory Investigation:
Student volunteers will be recruited from the University of Cambridge via email to college and society email lists. Volunteers will be screened for eligibility via email, and then will attend the PAVE Imaging and Performance Laboratory (PAVE-IPL). Eligible volunteers will give informed consent, before having anthropometric measurements (height, mass, upper limb measurements) taken using standard protocol (Norton and Olds, 1996; Cameron, 2013), 2D and 3D hand scans, 3D body scans (Sizestream Inc, 2014), and bioelectrical impedance analysis data collected from them(Tufts University Nutrition Collaborative, 2003). They will then have a thermal image taken of their hands using a FLIR T460® camera (FLIR Systems, 2015). They will then undergo brief dexterity tests on both hands using established protocol for the Purdue Pegboard (Daanen, 2009). Participants will then immerse their hands in cold water (5˚C) for a maximum of 3 minutes. After 3 minutes the participant will remove their hand from the water, rate the cold/pain sensation as a safety precaution, and have a second thermal image taken of their hands, and then repeat the dexterity test. 3 minutes was chosen for cold-water-immersion as this is a time known to induce a vasoconstriction response to cold, but prior to cold-induced vasodilatation response and cold injury (Mekjavic et al., 2008).
Participants will then be allowed rest time, a hot/cold drink and snack of their choice and will be free to leave.
Nepal Field Investigation:
Volunteers of self-identified Sherpa origin in Namche Bazaar, Nepal, and volunteers of self-identified Tibetan ancestry in Kathmandu, Nepal, will be recruited during direct meetings during the Caudwell Xtreme Everest 2017 Research Expedition. Volunteers will be screened for eligibility through verbal communication. Eligible volunteers will give informed consent before having anthropometric measurements (height, mass, upper limb proportions) taken using standard protocol (Norton and Olds, 1996; Cameron, 2013) at either the Namche Bazaar Health Post, Namche Bazaar Monastery, or Jawalakhel

Question 9a: Does the study involve any pharmaceutical or other compounds with physiological effects?

No

Question 10: What ethical issues does this study raise and what measures have been taken to address them?

Laboratory Investigation
Immersion of one's hand in cold water is likely to result in temporary discomfort in the form of cold/pain sensation. Individuals are informed that they may withdraw from the investigation at any time if they reach a level of discomfort which they do not wish to be in. Cold immersion for 3 minutes is considered a safe immersion time as it is not long enough for tissue damage to occur.
No other conditions in the laboratory investigation cause discomfort or inconvenience.
Nepal Investigation
Measurement of the body may be considered unethical in some communities in Nepal. Thus, to ensure that all standard anthropometric procedures are culturally sensitive, all volunteers will have the procedure explained to them prior to measurement, and volunteers can withdraw at any time. Participants will also be measured through light clothing to minimise any participant discomfort.

Question 11: Who will the participants be?

UK Laboratory Study
The participants will be healthy volunteers ages 18-50 from the student and residential population of Cambridge. I plan to recruit approximately 200 volunteers. Volunteers will be ineligible if they suffer any of the following conditions:
Raynaud's disease, or other cold-related injury
Hypothermia
Cold-related asthma
Type I/II diabetes
These conditions will not be tested, as they are either known to affect peripheral circulation.
Women who are pregnant or breastfeeding will also be ineligible for this study.
Individuals who have a cardioverter defibrillator implant will also be ineligible for this study, as they have yet to be tested for safe use with bio-impedance analysis equipment.
The age limit of 50 is in place, as control of peripheral circulation has been shown to decrease with age (Guergova and Dufour, 2011)
Nepal Field Study
Highland Sample: The participants will be healthy volunteers ages 18-60 from Namche Bazaar, of at least third generation Sherpa ancestry. I plan to recruit approximately 100 Sherpa volunteers. Confirmation of Sherpa ancestry will be both through self-identification and through identification documents such as school records or birth certificates where possible
Lowland Sample: The participants will be healthy volunteers ages 18-60 from Kathmandu, recruited through the Jawalakhel Tibetan Community Centre. Confirmation of Tibetan ancestry will be both through self-identification and through identification documents such as school records or birth certificates where possible.

Question 12: Describe the recruitment procedures for the study

Laboratory Investigation

A flowchart of recruitment procedures can be found below. Participants will be invited via email to college and society lists. Any individuals who respond to the email will be sent the PARTICIPANT INFORMATION SHEET (accompanying this application), and STUDY CONDUCT INFORMATION SHEET (accompanying this application), and will be offered several investigation slots to choose from, along with highlighting the ineligibility criteria, so that volunteers can self-select as to whether they are eligible for the study. If the volunteer replies to indicate a time slot preference, this will then be confirmed via email by the research team, along with details of what to bring and wear. Participants will then attend the PAVE-IPL in their designated time slot.

Nepal Field Investigation

Participants will be recruited directly during meetings and gatherings held by the Caudwell Xtreme Everest Team, in both Namche Bazaar and Kathmandu. Participants will be information verbally in English, Sherpa, Tibetan or Nepali.

Question 13: Describe the procedures to obtain informed consent

Laboratory Investigation

Participants will be given a printed copy of the PARTICIPANT INFORMATION SHEET, STUDY CONDUCT INFORMATION SHEET, and CONSENT FORM & QUESTIONNAIRE (accompanying this application), which states that the participant has read and understands the study procedure, the risks, benefits and possible outcomes. The participant's signature is required on the CONSENT FORM & QUESTIONNAIRE, prior to involvement in the investigation.

Nepal Field Investigation

Participants will sign (or thumb print if illiterate) a CONSENT FORM, and verbally answer a questionnaire prior to involvement in the investigation.

Question 14: Will consent be written?

Yes.

Question 15: What will participants be told about the study? Will any information on procedures or the purpose of study be withheld?

Participants will be informed of the entire study procedure, risks, benefits and possible outcomes. No information will be withheld, in the **Laboratory Investigation** and **Nepal Field Investigation**. Participant's questions will be answered fully.

Question 16: Will personally identifiable information be made available beyond the research team?

No

Question 17: What payments, expenses or other benefits and inducements will participants receive?

Laboratory Investigation: All participants will be offered a hot drink (tea or coffee), a choice of fruit and a choice of chocolate or cereal bar during the study.
Nepal Field Investigation: All participants will be offered a choice of chocolate or confectionary on completion of the study.

Question 18: At the end of the study, what will participants be told about the investigation?

Participants have the following debrief stated to them (for the Nepal Investigation, in Nepali if required):
"Thank you very much for participating in our study. If you have any concerns or questions, please feel free to contact the research group at any time. We want to confirm that all the data collected will remain strictly anonymous. If you would like us to inform you of any publications or presentations the data from this study is used in then please feel free to ask and we will update you. If you have any questions now, please do ask us and we will do our best to answer any questions. If you have no questions, you are free to leave, you have completed the study. Many thanks again for your participation."

Question 19: Has the person carrying out the study had previous experience of the procedures? If not, who will supervise that person?

Stephanie Payne (SP) will by the primary investigator. SP has previous experience in collecting anthropometric data from undergraduate research. SP will be given training by Dr Daniel Longman and Dr Alison Macintosh on the use of the equipment used in the PAVE-IPL, including the use of the SizeStream 3D scanner and the bioelectrical impedance analysis equipment. SP will be trained by a representative of Artec 3D Systems, on the use of the portable 3D scanner. SP will be trained in use of the thermal imaging camera by Dr Jurgi Cristobal Azkarate. No training is required for use of the hand dynamometer and Purdue Pegboard. Furthermore, the procedures will have been practised to ensure familiarity and accuracy of data collection.

Question 20: What arrangements are there for insurance and/or indemnity to meet the potential legal liability for harm to participants arising from the conduct of the study?

Insurance has been obtained for this investigation (evidence accompanying this application)

Question 21: What arrangements are there for data security during and after the study?

Stephanie Payne and Dr Jay Stock **only** will have access to the participants' personal data. All forms will be filled out by hand. All collected data, forms and questionnaires will be kept strictly confidential and secure in locked filing cabinets. Each participant will be assigned a unique, linked-anonymising code to ensure that personal information is not directly linked to any data or results. Personal information will be destroyed 12 months after the project has ended. Consent will be attained for retention of data, but not personal information, for future studies. Data will be destroyed after 20 years. Participants can request to have their data destroyed at any time. Participants can also request copies of any data collected specific

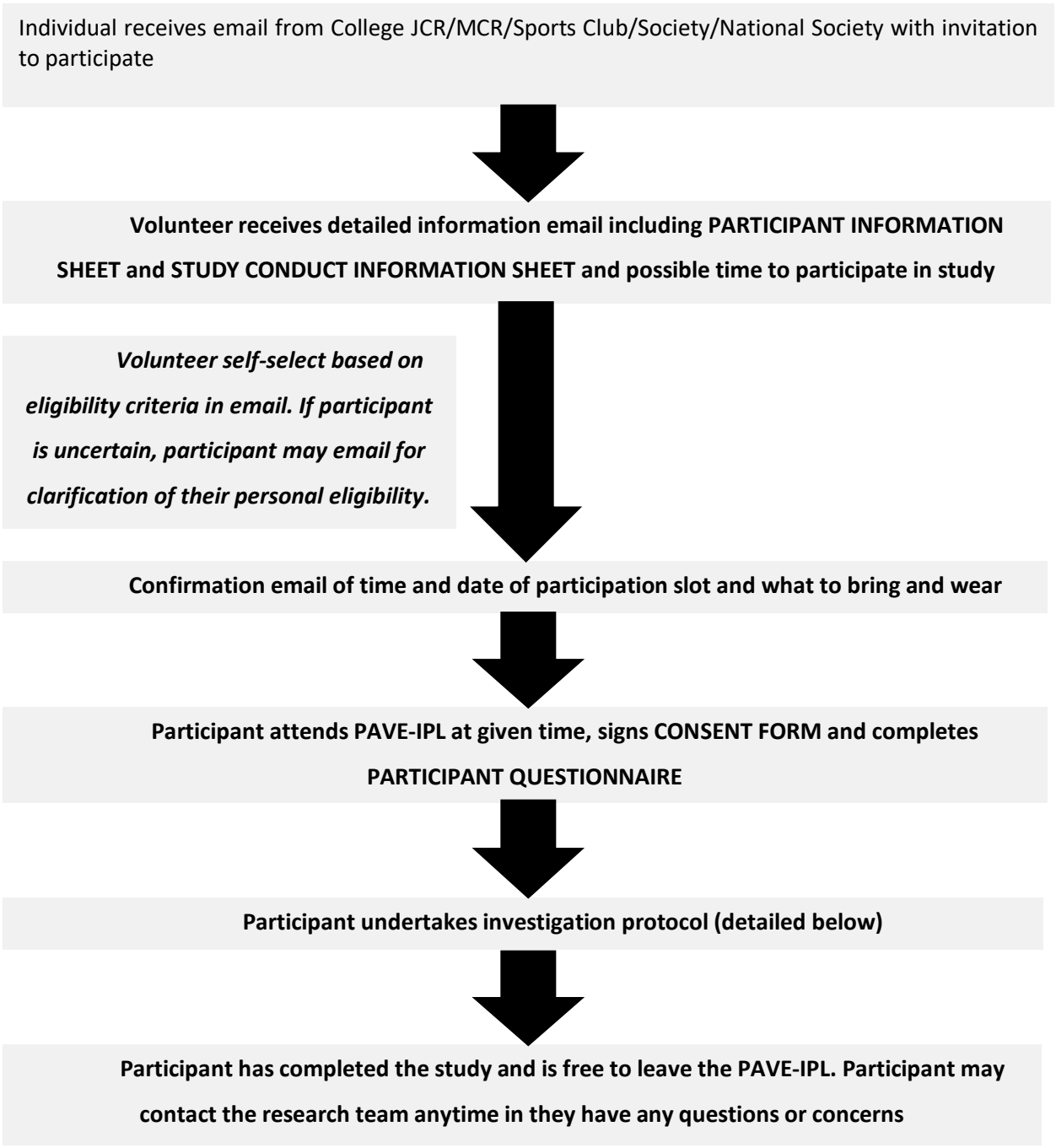
Signatures of the study team (including date)

Signatures of the study team (including date)


Stephanie Payne 08/08/2016


Jay Stock 08/08/2016

Recruitment Flowchart for Laboratory Study



The invitation email will read as follows:

BioAnth Study: Participate for free chocolate and coffee

Hi there,

The Department of Biological Anthropology are looking for healthy volunteers to participate in a study looking at how hand and foot coordination changes with brief exposure to cold.

You will carry out a brief coordination test before and after immersing your hands and feet in cold water for 3 minutes. You will be rewarded with a selection of chocolate, fruit and a hot drink of your choice (tea/coffee/hot chocolate)!

Investigation: Coordination and Thermoregulation

Location: Department of Biological Anthropology, Pembroke Street, CB2 3DZ

Experiment: Approximately 1 hour

Who can participate: Healthy volunteers

For further information, please contact:

Stephanie Payne (sp627@cam.ac.uk)

After initial interest has been shown, the following email will be sent detailing the procedure and possible attendance dates and times:

Coordination and Thermoregulation Investigation

Hi (insert volunteer's name),

Thank you for showing interest in the Coordination and Thermoregulation Investigation, run by the PAVE Research Group in the Division of Biological Anthropology.

Please read the attached Participant Information Sheet and Study Conduct Information Sheet. After reading these information sheets, if you do indeed decide that you wish to participate, please reply to this email, indicating which of the following dates and times would suit you to visit the PAVE Imaging and Performance Laboratory on Pembroke Street, CB2 3DZ.

Possible investigation slots: _____

Please note that if you have had any of the following health conditions, you will unfortunately not be able to participate in this study:

- *Raynaud's disease/other cold-related injury*
- *Hypothermia*
- *Cold-related asthma*
- *Type I/Type II diabetes*
- *Cardioverter defibrillator implant*

Once we have received your reply, we will email to confirm your investigation slot and details of what to expect on the day.

We very much look forward to hearing from you,

The PAVE Research Team

The conduct sheet, participant information sheet, and participant questionnaire can be found below:

Dexterity and Thermoregulation

STUDY CONDUCT INFORMATION SHEET

PAVE Research Group
Stephanie Payne | Dr Jay Stock
Imaging and Performance Laboratory | University of Cambridge | Cambridge | CB2 3QG

This sheet gives information on confidentiality and data protection, indemnity and compensation, publication, etc. It is important that you have read the information found here, alongside the* PARTICIPANT INFORMATION SHEET*. Please take time to read this information sheet carefully and ask us if there is anything unclear, or if you would like further information. Please take time to decide whether or not you wish to take part in this study.

Will my taking part in this study be kept confidential?

Yes - any information that is collected about you during the course of the research will be kept strictly confidential: PAVE-IPL will be the custodians of the data. Any information about you that leaves PAVE-IPL will have your name and address removed so that you cannot be recognised from it.

A standard confidentiality procedure is in place for participants involved in research. This stipulates how personal information is collected, used, stored and disposed of during and following completion of research projects. Any information that is collected about you during the course of the project will be kept strictly confidential and secure in locked filing cabinets and or/electronic files on computers that have restricted access. Each participant is assigned a unique, linked-anonymising code to be used for all data collected during the research. Personal information will not be linked to any data or results. Once the study is over, the data will be completely anonymous.

Only the specified research team will have access to personal identifying data information. PAVE-IPL maintains a central record of all research projects but this does not include personal information on participants, which will be kept no more than 12 months after the project has ended. With your agreement, non-personal data will be stored for 20 years. With your consent, and with the appropriate research ethics approval, retained data may be used for future studies.

What will happen to images, scans, data and questionnaire information collected?

Any images, scans, data, and questionnaires that are collected during the course of the project will be processed and kept in accordance with PAVE-IPL standard operating procedures. Each participant is assigned a unique, anonymising code to be used to label all data and questionnaires collected during the research. Personal information will not be linked to any saved data. Only the specified research team will have access to your data and questionnaires. With your agreement, we may store data for up to 20 years and then they will be destroyed. With your consent, and with the appropriate research ethics approval, retained data may be used for future studies.

What will happen to my data if I do not want to carry on with the study?

If you decide to withdraw from the study, with your consent, data obtained may be kept and used to contribute to study results or, with your consent, for future studies. However, should you request your data to be destroyed along with any other information relating to you, we will ensure that this takes place.

What will happen to the study results?

The overall study results may be presented at scientific meetings or published in a scientific journal. You will not be identified in these presentations and publications. We will be happy to discuss the results with you at the end of the study if you wish.

What should I do if I am harmed during the study?

If you are harmed and this is due to someone's negligence then you may have grounds for legal action for compensation against the University of Cambridge, but you may have to pay for legal costs. For research carried out at the University of Cambridge, participants would be in the same position as if public liability insurance had been taken out.

The University of Cambridge undertakes to give sympathetic consideration, on a case by case basis, to claims of negligent and non-negligent harm arising from research carried out at the University provided the claim does not relate to standard treatment.

What should I do if I want to make a complaint?

Any complaints about the way you have been dealt with during the study or any possible harm you might suffer will be addressed and fully investigated. If you have a concern about any aspect of this study, you should speak with Stephanie Payne, Alison Macintosh, Danny Longman, or Jay Stock who will do their best to answer your questions. If you remain unhappy and wish to complain formally, please contact:

Professor Charles French

Head of Department, Archaeology & Anthropology, University of Cambridge

+44 (0)1223 333533

Who should I contact for further information?

If you have any further questions or if you have any concerns whilst participating in the study, please contact **Stephanie Payne (sp627@cam.ac.uk)**, and/or **Dr Jay Stock (jts34@cam.ac.uk)** at PAVE.

Dexterity and Thermoregulation

PARTICIPANT INFORMATION SHEET

PAVE Research Group
Stephanie Payne | Dr Jay Stock
Imaging and Performance Laboratory | University of Cambridge | Cambridge | CB2 3QG

You are being invited to take part in a research study. This information sheet tells you about the purpose of the study and what will happen if you agree to take part. Details about the conduct of the study, confidentiality and data protection, indemnity and compensation, publication etc. are provided on the* STUDY CONDUCT INFORMATION SHEET*. Please take time to read both of these information sheets carefully and discuss them with others if you wish. Please ask us if there is anything which is unclear, or if you would like further information.

What are the aims of the study?

This study aims to find out how the proportions of our hands influence our dexterity in hot and cold conditions. By taking measurements of the hand relative to the rest of the body, and performing manual tasks after brief cold exposure, we can build a picture of the body's dynamic thermoregulatory responses and how they might vary according to our body type and previous cold exposure.

Why have I been invited?

We are contacting you because you have been identified as a healthy adult above the age of 18.

Do I have to take part?

It is your decision whether to take part in the study or not. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw at any point in the study without giving a reason, and this will not affect your legal rights or the standard of care that you receive.

What will happen to me if I take part?

You will be invited to attend the PAVE Research Group Imaging and Performance Laboratory (PAVE-IPL) at the Department of Archaeology and Anthropology. Your visit will last approximately one and a half hours.

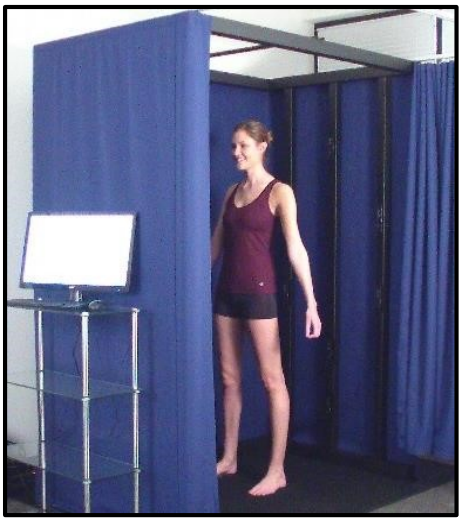
Might I be excluded from the study?

You may not be eligible to take part in some aspects of the study if you have a cardioverter defibrillator implant or you suffer from photosensitivity/epilepsy. A member of the research team will ask you if this is the case, and if so, will emit these aspects of the study procedure for you. You will be able to take part in all other aspects of the study.

What do I have to do?

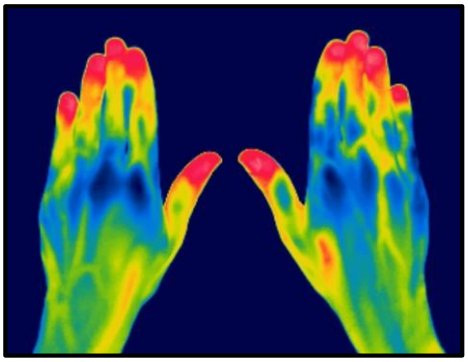
1: Questionnaire and Consent form - At the PAVE-IPL, you will fill out a questionnaire and be asked to sign the consent form.

2: Full Body 3D Scanning - You will be asked to stand still in a scanning booth (see Picture 1) for approximately two minutes while a 3D scan is taken of your body. The scan takes thousands of measurements automatically, and is painless and does not involve any radiation.



3: Body Measurements - You will have your height, weight and several arm and finger measurements taken.

4: Body Composition Analyses - You will be asked to step on to a platform to calculate your body composition (the amount of bone, fat and muscle in your body). It is not recommended that you carry out this element of the study if you have a cardioverter defibrillator implant. Please make the research team aware if this is the case.



5: 2D Hand Scanning – You will be asked to place both your hands on a photocopier scanning plate, whilst we take three scans of your hands.

6: Hand and Arm 3D Scanning - You will then be asked to sit whilst we take 3D scans of your hands and arms. This will take several minutes and is also painless and involves no radiation. This scan involves bright, flashing lights, so please make the research team aware if you are photosensitive.

7: Thermal Imaging - You will have a series of photographs taken of your hands throughout the investigation using a thermal imaging camera (see Picture 2).

8: Dexterity Test - You will have your dexterity tested, where you will be asked to place as many pins in a pinhole board in a set time (see Picture 3).

9: Immersion Test - You will be asked to put on non-latex gloves and immerse your hand in cold water for 3 minutes. You will be asked to rate how cold your hands feel. After 3 minutes, your hand will be removed from the cold water,

gloves also removed, and a second thermal image taken. You will then be asked to repeat the dexterity test.

What will I have to wear?

Please arrive at the PAVE-IPL in comfortable clothing. For the 3D body scan, you will be asked to wear close-fitting clothing as the scanner uses the external outline of your body to make 3D images, and thus any clothes you wear will be included in your outline. There will be a private changing area available for you to change into close-fitting clothing. For the rest of the study, you can wear comfortable clothing.

What are the possible risks of taking part?

There are no risks associated with body measurements, 3D scanning, body composition analysis, or thermal imaging. There are also no risks associated with short-term exposure of the hands to cold water. However, you may experience mild discomfort during the immersion period. You can withdraw from the experiment at any point if you reach a level of discomfort which you do not wish to be at.

What are the possible benefits?

Your participation in this study will increase our knowledge of thermoregulation. You can request to have a copy of your 3D scans, thermal images and other information sent to you. You will be provided with chocolate, and a free hand-warmer pack on completion of the study. There will be no other direct benefit to you.

What will happen if anything goes wrong?

In the unlikely event that something should go wrong during the study, procedures will be stopped. Standard procedures are in place at the PAVE-IPL, while acting as the research site, for dealing with serious adverse events should they occur.

Any complaints about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given on the **STUDY CONDUCT INFORMATION SHEET**. If you have any concern or need further details at any point, please contact **Stephanie Payne (sp627@cam.ac.uk)** or **Jay Stock (jts34@cam.ac.uk)**.

Who is organising and funding the study?

This study is being organised by the PAVE Research Group, Department of Archaeology & Anthropology. This study is funded by the European Research Council and Trinity Hall, Cambridge.

Dexterity and Thermoregulation

CONSENT FORM

Cambridge University HBREC Reference Number: HBREC.2016.22

Please tick

- ☐ I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions.
- ☐ I understand that data will be linked-anonymised, personal information will not be linked to any data.
- ☐ I understand that data from this study will be presented at conferences and published in journals. The data presented will be anonymous.
- ☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my legal rights being affected.
- ☐ I understand that being exposed to cold water may temporarily cause mild discomfort.
- ☐ I understand that there are bright flashing lights involved in the scanning process, and take full responsibility for making the research team aware of any photosensitivity condition I may have.
- ☐ I understand that this project has received ethical approval from the Cambridge University Human Biology Research Ethics Committee.
- ☐ I consent to my anonymised data being used for future studies, for a maximum of 20 years.
- ☐ I agree to take part in the above study.

Name of Volunteer *(Please print)*	Date	Signature
Name of Research Team Member *(Please print)*	Date	Signature

2 copies required: for researcher and volunteer

Dexterity and Thermoregulation

Screening Questionnaire

Participant _ _ _ *(completed by research team)* Date of Birth _ _ / _ _ / _ _ _ _

Email _____ Contact Number _____

Address _____

Have you ever had a cardioverter defibrillator implanted? **Yes/No**

Have you ever had any of the following health conditions? ***Delete as appropriate***

Cold injury	**Yes/No**	Hypothermia	**Yes/No**
Raynaud's disease/Poor circulation	**Yes/No**	Type I/II diabetes	**Yes/No**

If you have answered **Yes** to any of the above, please provide further details

_____

If you smoke, do you smoke more than 10 cigarettes a week? **Yes/No**

FEMALE PARTICIPANTS ONLY: Are you currently pregnant or breastfeeding? **Yes/No**

Date _ _ / _ _ / _ _ _ _ Participant _ _ _ *(completed by research team)*

Handedness and Occupation

Are you left or right handed? *Delete as appropriate* **Left/Right**

Occupation _____

Birth Place

In which town/city were you born? _____

In which town/city was your mother born?_____

In which town/city was your father born? _____

On receipt of confirmation email from the volunteer the following email will be sent:

Details for Coordination and Thermoregulation Investigation

Hi (insert participant's name),

Thank you for indicating your availability for our study. We would like to invite you to the PAVE Imaging and Performance Laboratory on Pembroke Street, CB2 3DZ. Attached is a map to the laboratory, and a member of the research team will be there to meet you at the entrance.

You are provisionally booked to attend at: (hh:mm, DD/MM/YY)

If this is no longer convenient for you then please reply to this email and we will arrange a time that is better suited to you.

Please come in comfortable clothing and bring close-fitting clothes to be worn in the 3D body scanner. The scanner uses the external outline of your body to make 3D images, and thus any clothes you wear will be included in you outline. To ensure that an accurate representation of your body outline is obtained, men should wear lycra shorts and no shirt; women should wear lycra shorts and a sports bra or fitted vest. Please also wear cotton underpants, which will be worn under standard clothing during immersion testing. If you will have difficulty bringing you own clothing, please reply to this email, and the team will do their best to provide suitable clothing for you.

Please ensure that you are well hydrated, and have not exercised or been in a sauna 8 hours before the time you are due to attend the laboratory. We ask that you have not imbibed alcohol or caffeinated drinks 12 hours before you are due to attend the laboratory.

We very much look forward to seeing you at the PAVE-IP Laboratory.

Kind regards,

The PAVE Research Team

Laboratory Protocol

- Participants will be asked to change into close-fitting clothing in the private changing area and to remove socks, shoes and any jewellery other than stud earrings after consent.
- The observer will familiarise the participant with the procedure by demonstrating on the observer, or another member of the research team if present.

Anthropometry

- Standard anthropometric procedures followed (Norton and Olds, 1996; Cameron, 2013).
- Weight: Participant stands on the centre of weighing platform. Record the weight to 0.1kg.
- Height: Participant stands on the platform of the Seca Leicester Height Measure with their back to the vertical board. Weight evenly distributed across the feet, heels placed together, both heels touching the base of the vertical board, feet should ideally point 60˚ degrees outwards. The buttocks, scapulae and head are positioned in contact with the vertical backboard where possible, arms hanging freely, palms facing the thighs, and head facing forward. On an in-breath, the horizontal bar should be lowered to sit snugly on the crown of the participant's head with sufficient pressure to compress hair. Record height to the nearest mm.
- Humerus Length: Participant stands and rolls up the sleeve of the right arm. Participant flexes arm to 90˚ to the floor. The acromion lateral tip is marked with body marker. The inferior border of the olecranon process is marked with body marker. Standing on the right side of the participant, with the sliding callipers in the right hand, place the counter blade on the marked acromion and the fixed blade on the marked olecranon. Record upper arm length to the nearest mm.
- Ulna Length: The distal end of the styloid process is marked with body marker. The counter blade is applied to the marker olecranon and the fixed blade to the styloid process. Record fore-arm length to the nearest mm.
- 2D Hand Scan: Participant places their right hand on the scanning plate of the CanoScan LiDE 600 Scanner, palm facing downwards. One image is taken with fingers together; one image is taken with fingers spread as widely as possible.
- 3D Hand Scan: Participant sits with the right arm abducted parallel to the ground, fingers outstretched but held together, thumb held away from the fingers. Open *Scan* panel on the desktop. Hold scanner 0.5m away from at same height as hand, pointing at the thumb. Press *Record* button on scan panel and move around the hand 180˚, remaining 0.5m away. Continue up the arm to the acromion process on the shoulder. Press *Stop* button on scan panel once a 3D scan of the entire hand has been collected.

- SizeStream: Standard measurement procedure followed (Sizestream Inc, 2014). Participant steps into the body scanner, observer closes curtain behind them. Participant told to stand on footprint marks, feet approximately shoulder-width apart and toes pointed out to ensure complete foot coverage. Participant grasps adjustable handhold with the right hand. Handhold will slide so the participant is standing upright in a normal relaxed posture while holding the handhold. The left arm should be held away from the body similar to the right arm's position. Observer asks for confirmation that participant is ready for Scan. Observer enters participant number, click the grey button under the Sizestream logo. Audio instructions will be given to the participant. The scan is carried out. After the scan, the participant is told to relax whilst observer checks the scan. If the scan is approved, then participant handed standard test clothing to put on.
- Body Composition Measurement: Participant will stand on SECA mBCA-515 body composition analyser, with heels on heel pads, toes on toe-pads, and fingers gripping finger pads. The analyser will be switched on to measure fat-free mass, fat mass, and skeletal muscle mass for the participant.

Thermoneutral Tests

- Each participant will enter testing room, which is held at a given room temperature (24˚C).
- They will be asked to sit and have core temperature taken using the Braun Thermoscan to 0.1 ˚C.
- The temperature of each hand will be taken using a thermal imaging camera FLIR T460®. The hand will be placed with fingers outstretched on a plastic table top whilst the image is taken.
- The participant will then have the procedure explained to them. After 10 minutes, body temperature will be taken again, to determine whether their body temperature is stable.
- A second thermal image will be taken of each hand to determine whether hand temperature is stable. The investigation will then commence.

Finger Dexterity

- Carry out dual dexterity test as stated by Purdue Pegboard Instructions (Parkway and Box, 2002)

Immersion Tests

- The participant will then have their body temperature, and hand temperature measured again prior to immersion using the Braun Thermoscan.
- One thermal image will be taken.

- The participant will then put latex-free gloves on their hands before immersing their hands in a bucket of ice-cold water (0˚C), up to the styloid process, but not over the top of the gloves.

Post-Immersion

- At the end of the 3-minute period, the participant will be asked to rate the cold sensation on an 11 point scale (0-not cold, 10- extreme cold), and pain sensation on an 11 point scale (0-no pain, 10- extreme pain).
- The participant will remove the gloves and have a thermal image taken immediately. Then they will repeat the Purdue pegboard test.
- The participant will then proceed to the private changing area where they will change back into their own clothing
- Participants will then be offered a glass of water and a choice of fruit/cereal bar or chocolate.
- Participant is free to leave.

Protocol for Nepal Field Investigation

Consent

- On attendance of the Jawalakhel Community Centre/Namche Bazaar Health Post/Namche Monastery, the participant will be informed of the protocol and given the Questionnaire Consent Form to read and complete. The form is below:

UNIVERSITY OF CAMBRIDGE सहमति फर्म Consent Form PAVE Participant

Number: .....सि.यु HBREC रेफरेन्स नम्बर: 2016.22 नेपाल स्वास्थ्य अनुसन्धान परिषद रेफरेन्स नम्बर: 1571

म पुष्टिगर्छु कि मैले माथि उल्लेखित अध्ययन सम्बन्धि जानकारी पत्र पढे र बुझे र मलाई प्रश्नहरु सोध्ने अवसर प्राप्त भएको थियो ।

I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions

मैले बुझेको छु कि मेरो व्यक्तिगत पहिचान कुनैपनि तथ्यांकसगँ मिलाइने छैन। मेरो तथ्यांक व्यक्तिगत पहिचान बिना भविश्यमा ९२० वर्षसम्म हुने अनुसन्धानमा प्रयोग हुन सक्नेछ।

I understand that data will be anonymized, personal information will not be linked to any data, and that my data may be used for future studies, for a maximum of 20 years.

मैले बुझेको छु कि मेरो सहभागिता स्वयंसेवकको रुपमा हुनेछ र म कुनै पनि बेला यस अध्ययनबाट आफुलाई कुनै कारण नदिइकन अलग गर्न सक्नेछु। मैले पाउने कानुनी संरक्षण उलंघन हुने छैन।

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my legal rights being affected.

मैले बुझेको छु कि यो अध्ययन परियोजनाले केमब्रिज विश्व विद्यालयको मानव जिवशास्त्र अनुसन्धान इथिक्स समिति र नेपाल स्वास्थ्य अनुसन्धान परिषदबाट इथिकल स्वीकृती लिएको छ ।

I understand that this project has received ethical approval from the Cambridge University Human Biology Research Ethics Committee and the Nepal Health Research Council.

माथि उल्लेखित अध्ययनमा भाग लिन म सहमत छु ।

I agree to take part in the above study.

……__ __/__ __/2017 ……

सहभागीको नाम (कृपया लेख्नुहोस) मिति Date सहि Signature

- The observer will familiarise the participant with the procedure demonstrating on themselves
- Ensure participants are wearing light clothing, no shoes

Anthropometry

- Standard anthropometric procedures followed (Norton and Olds, 1996; Cameron, 2013).
- Weight: Participant stands on the centre of weighing platform. Record the weight to 0.1kg.
- Height: Participant stands on the platform of the Seca Leicester Height Measure with their back to the vertical board. Weight evenly distributed across the feet, heels

placed together, both heels touching the base of the vertical board, feet should ideally point 60˚ degrees outwards. The buttocks, scapulae and head are positioned in contact with the vertical backboard where possible, arms hanging freely, palms facing the thighs, and head facing forward. On an in-breath, the horizontal bar should be lowered to sit snugly on the crown of the participant's head with sufficient pressure to compress hair. Record height to the nearest mm.

- Humerus Length: Participant stands and rolls up the sleeve of the right arm. Participant flexes arm to 90˚ to the floor. The acromion lateral tip is marked with body marker. The inferior border of the olecranon process is marked with body marker. Standing on the right side of the participant, with the sliding callipers in the right hand, place the counter blade on the marked acromion and the fixed blade on the marked olecranon. Record upper arm length to the nearest mm.
- Ulna Length: The distal end of the styloid process is marked with body marker. The counter blade is applied to the marker olecranon and the fixed blade to the styloid process. Record fore-arm length to the nearest mm.
- Hand Length: Participant sits with right arm forearm resting on the table, palm facing upwards, fingers and palm fully extended and hand flat. The fixed blade of the calliper is placed against the most distal point of the middle finger; the sliding blade is placed on the marked styloid process. Record hand length to the nearest mm.
- Hand Width: Participant holds hand with the identical position to the previous measurement. The fixed blade is placed on the distal side of the fifth metacarpophalangeal joint, and the sliding blade is placed on the proximal side of the second metacarpophalangeal joint. Record hand width to the nearest mm.
- All measurements were recorded on the following form:

UNIVERSITY OF CAMBRIDGE **Scientific Study of Human Hands** PAVE

Date *(DD/MM/YYYY)* _ _ / _ _ / _ _ _ _ Participant Number ……

Age *(in complete years)* …… Birthplace ……

Migration *(if applicable)*……

Handedness **L/R** Occupation ……

Ethnicity and town/region of parents and grandparents' origin: **Same/Different**

Notes:

……

Number of siblings:……

Any amputations/bone fractures? ……

Body Weight (kg) _ _ _ /_ _ _/ _ _ _ Body Height (mm) _ _ _ /_ _ _/ _ _ _

Humerus Length (mm)_ _ _ /_ _ _/ _ _ _ Ulna Length (mm) _ _ _ /_ _ _/ _ _ _

Hand Length (mm) _ _ _ /_ _ _/ _ _ _ Hand Width (mm) _ _ _ /_ _ _/ _ _ _

- After measurement, participants will be offered a choice of confectionery or chocolate
- Participant is free to leave

The following form demonstrates evidence of insurance for this investigation:

UNIVERSITY OF CAMBRIDGE
Finance Division

Head of Insurance

Our Ref: 609/M/C/1728

Dr Jay Stock

Department of Archaeology and Anthropology

University of Cambridge

14th October 2016

Dear Dr Stock

How does dexterity change in cold stress, heat stress and at high altitude?

I am writing to confirm that, on the basis of information supplied this research will be covered by Newline Clinical Trials policy B0823Q31000177 which has a £10m Limit of Indemnity.

The University's insurance is primarily concerned with the risks associated with 'design of study protocol', however the cover extends to claims made on a non-negligent harm basis.

This insurance indemnifies the University of Cambridge and its employees. There is no indemnity to NHS Trusts or Primary Care practices participating in this trial or to manufacturers of substances or equipment to be used in this trial.

Any amendments to the Study Protocol (including research sites) or to the Sponsorship of Study must be notified to the insurance section so that the insurance can be reviewed and ensure that all material facts are notified to the insurance underwriters as required by the insurance policy agreement.

Yours sincerely

P. P. V. Hellaby

Gill Armstrong

Greenwich House
Madingley Rise, Madingley Road
Cambridge
CB3 0TX

Ethical approval for the field study was also obtained from the Nepal Health Research Council (NHRC). The approval form is held by the NHRC, and thus is not available for publication in this thesis. However, the following letter demonstrates receipt of ethical approval from the NHRC:

Government of Nepal

Nepal Health Research Council (NHRC)

Ref. No.: 1571

01 March, 2017

Ms. Stephanie Alice
University of Cambridge
United Kingdom

Subject: Approval of Research Proposal entitled Testing hand and body proportions of high and low altitude populations in Nepal

It is my pleasure to inform you that the above-mentioned proposal submitted on 19 January 2017 (Reg.no. 14/2017 please use this Reg. No. during further correspondence) has been approved by NHRC Ethical Review Board on 01 March, 2017.

As per NHRC rules and regulations, the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective(s), problem statement, research •question or hypothesis, methodology, implementation procedure, data management and budget that may be necessary in course of the implementation of the research proposal can only be made so and implemented after prior approval from this council. Thus, it is compulsory to submit the detail of such changes intended or desired with justification prior to actual change in the protocol before the expiration date of this approval. Expiration date of this study is April 2017.

If the researcher requires transfer of the bio samples to other countries, the investigator should apply to the NHRC for the permission. The researchers will not be allowed to ship any raw/crude human biomaterial outside the country; only extracted and amplified samples can be taken to labs outside of Nepal for further study, as per the protocol submitted and approved by the NHRC. The remaining samples of the lab should be destroyed as per standard operating procedure, the process documented, and the NHRC informed.

Further, the researchers are directed to strictly abide by the National Ethical Guidelines published by NHRC during the implementation of their research proposal and submit progress report and full or summary report upon completion.

If you have any questions, please contact the Ethical Review M & E section of NHRC.

Thanking you,

.....

Dr. Khem Bahadur Karki - Member Secretary

Appendix 2 – Details of Field Investigation Populations

Details of the highland population

All participants in the highland population of the field study self-identified as Sherpa and all were born and resident in the Khumbu region of Nepal (Figure A2.1). The Sherpa were chosen for study as this ethnic group are associated with the Eastern Nepalese region of the high Himalayas (von Furer-Haimendorf, 1975), which they have occupied for approximately 300-400 years (Oppitz, 1974; Ortner, 1989). The Sherpa founding population stemmed from an ancestral Tibetan population (Bhandari et al., 2015). Using genetic estimates, the Sherpa population would have been relatively isolated for approximately 500 generations. The relative genetic isolation of the Sherpas makes them a suitable population of Tibetan ancestry, as many other Himalayan populations will have undergone extensive genetic mixing as a result of considerable migration in the region (Aldenderfer, 2016).

Sherpa livelihood is dictated by the harsh Himalayan environment. Sherpas have traditionally been pastoralists and agriculturalists, with a relatively limited diet (Stevens, 1993). This limited diet may well have acted as an energetic stress on the Sherpa phenotype, as indicated by Bailey *et al.* (Bailey and Hu, 2002; Bailey et al., 2007). Furthermore, the harsh environment of the Khumbu region will have produced additional energetic stress. Within the Khumbu region, the elevation varies from approximately 2800-8850m, creating an ecological gradient from temperate to alpine environments. The shallow soil, lack of nutrients, hypoxia (~15% atmospheric O_2 at 2800m, reaching as low as ~6% at Everest's peak), and cold conditions (falling to around -40˚C in winter), make the Everest region a very inhospitable place to live (Peacock, 1998). These conditions are also likely to have created high energetic demands on the Sherpa population which, when combined with a physically demanding pastoral/agricultural lifestyle, will have acted as a strong selection pressure on the Sherpa phenotype.

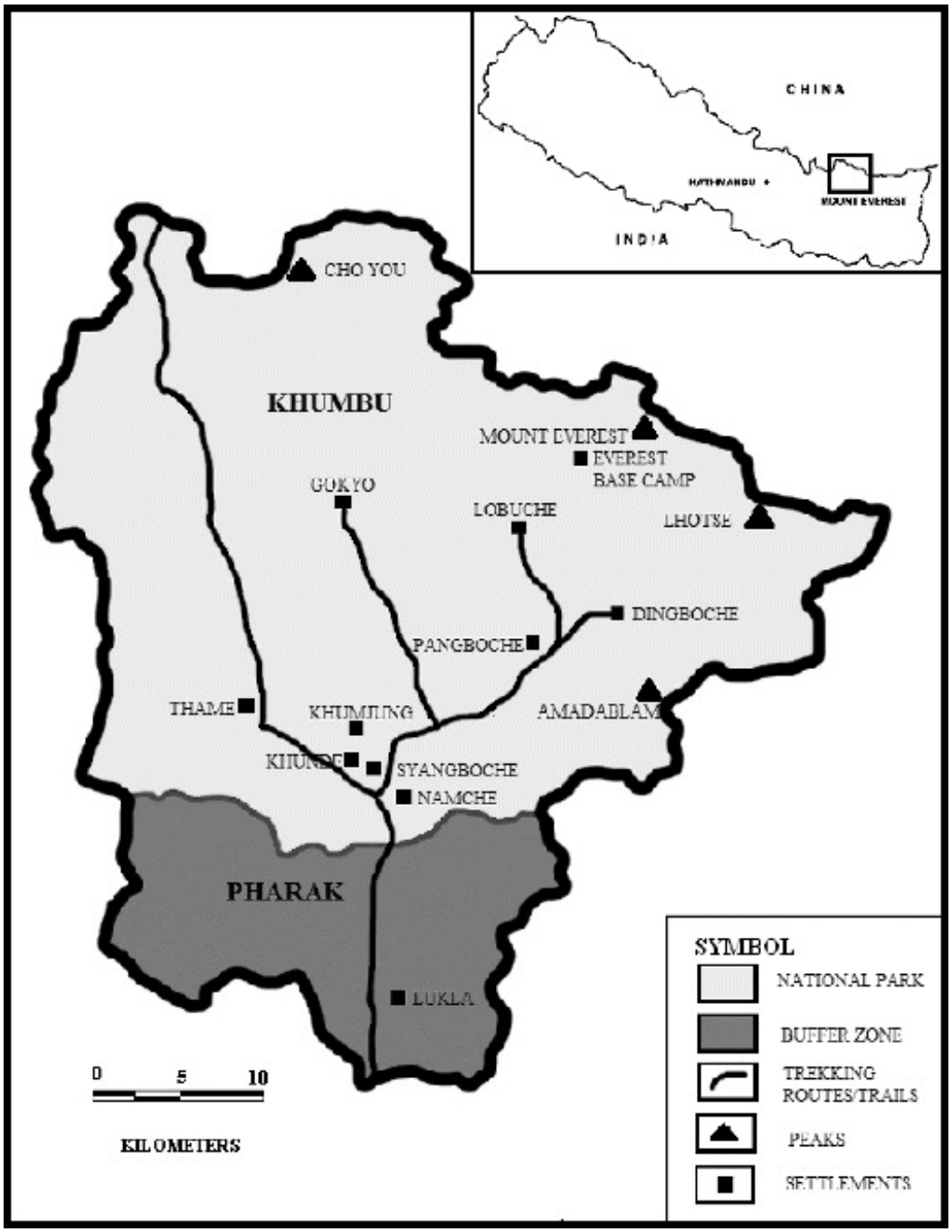


Figure A2.1 Map of Sagarmatha National Park (Nyaupane et al. 2014)

Details of the lowland population

The lowland population were of self-identified Tibetan origin, now living in the Jawalakhel refugee camp in Kathmandu. All participants had Tibetan ancestry, but had been born in either lowland Tibet during migration from the Tibetan Plateau to Nepal (Figure A2.2), or were born in Kathmandu. All participants were below the age of 58, to ensure that they were born after migration from the highland regions in Tibet in 1959 (Jian, 2006). Over 20,000 Tibetans migrated during this time as a result of persecution, including the exile of the Dalai Lama, and the subsequent Tibetan uprising.

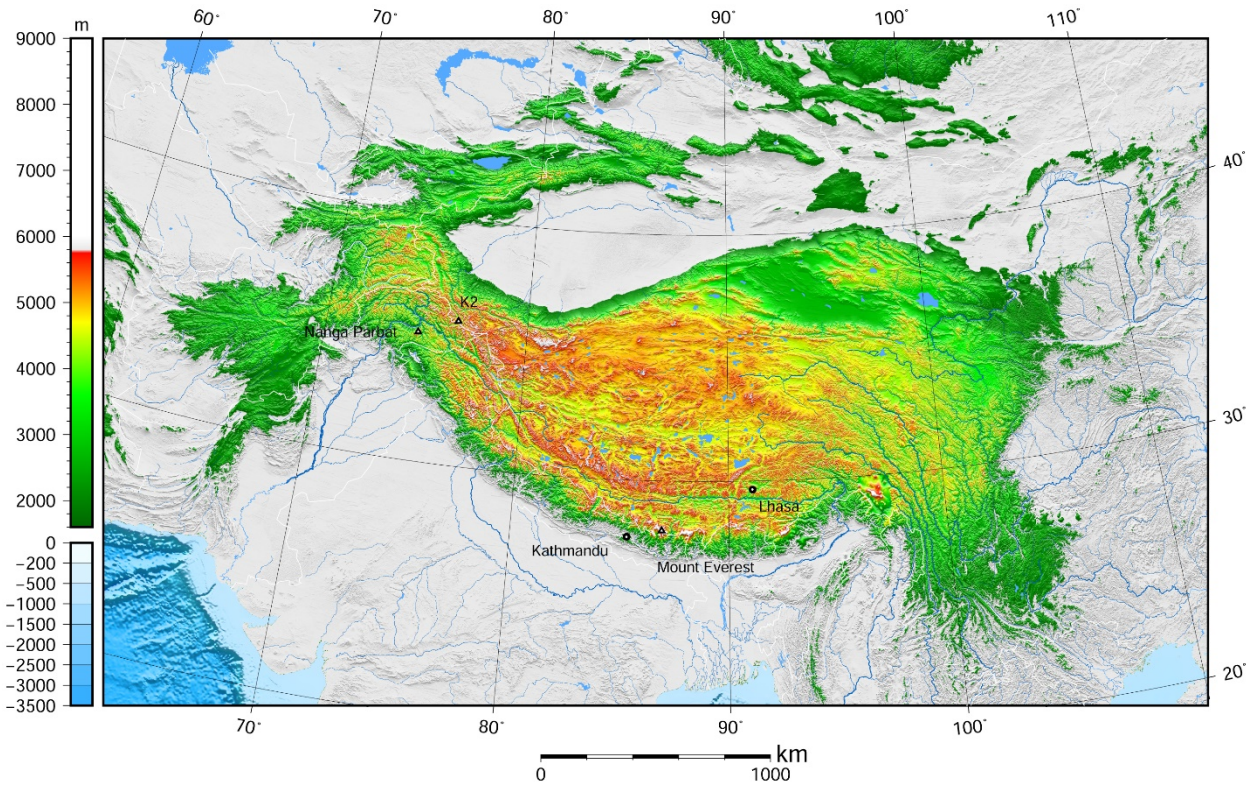


Figure A2.2 Topography of the Himalayas and the Tibetan Plateau.

This population were suitable as a lowland comparison to the Sherpa population as they had shared genetic ancestry (Bhandari et al., 2015), but had been residential at a relatively low altitude throughout their lives (~1800m), including childhood growth periods. Thus, this population will not have experienced the same altitude-associated stresses which the Sherpa population had been exposed to during growth.

Although this lowland Tibetan population may have been exposed to a westernised diet in Kathmandu, many of the participants affirmed maintenance of a traditional Tibetan Buddhist diet. This is similar to the Sherpa population, who may have been exposed to an increasingly westernised diet as a result of growing tourism in the Khumbu region. However, it was observed that most maintained a similar Buddhist diet.

In terms of physical activity, the populations were relatively well matched. The majority of the male Sherpa population measured were porters, whilst the majority of the male Tibetan population were factory workers in the Jawalakhel Tibetan community centre; both male samples having relatively high physical activity levels. The female Sherpa population were homemakers or lodge-hosts, whilst the female Tibetan population were either homemakers or shopkeepers, and so also had relatively similar activity levels.

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